

Systematic review and meta analysis

Work participation in patients with systematic lupus erythematosus: a systematic review

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Abstract

Objectives. This systematic review assessed which variables are associated with or are predictors for work participation outcomes in patients with systematic lupus erythematosus (SLE).

Methods. A literature search using MEDLINE, The Cochrane Library, Embase and CINAHL was conducted to identify all studies published from inception (1947) to June 2021 on factors related to and/or predicting employment status, absenteeism and/or presenteeism in SLE patients aged ≥ 18 years. The quality of included articles was assessed using the QUIPS tool. Narrative summaries were used to present the data.

Results. Fifteen studies (nine on associations, four on predictions, and two assessing both) were included, encompassing data of 3800 employed patients. Younger age, Caucasian ethnicity, higher educational level, lower disease activity score, shorter disease duration, absence of specific disease manifestations, higher levels of physical functioning and less physical job demands and higher levels of psychological/cognitive functioning were associated with or predicted favorable work outcomes. Older age, non-Caucasian ethnicity, female gender, never being married, poverty, lower educational level, higher disease activity score, longer disease duration, specific disease manifestations, lower levels of physical functioning, more physical job demands and low job control, less job tenure and lower levels of cognitive functioning were associated with or predicted an unfavorable work outcome. Limitations of the evidence were the quality of the studies and the use of heterogeneous outcome measures, applied statistical methods and instruments used to assess work participation.

Conclusion. We recommend applying the EULAR points to consider for designing, analysing and reporting on work participation in inflammatory arthritis also to SLE studies on work participation, to enhance the quality and comparability between studies and to better understand the impact of SLE on work participation.

Trial registration. registration in PROSPERO (CRD42020161275; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=161275).

Key words: systemic lupus erythematosus, prediction, work participation, absenteeism, presenteeism, employment

Rheumatology key messages

- Unemployment, absenteeism and presenteeism rates of SLE patients are higher than the general population.
- This systematic review summarised explanatory variables and predictors for work outcome in SLE patients.
- By identifying modifiable variables associated with reduced work participation, intervention strategies might be developed.

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the involvement of several organ systems, with a peak onset age during the reproductive years, leading to major restrictions in participation in all life areas, including work participation [1, 2]. As patients experience fatigue, reduced physical health, and may undergo intensive treatment, around half of all patients withdraw partly or entirely from the labour force at a young age [3–5]. Not participating in work may lead to lower self-esteem and possible financial problems for patients, and a high societal burden as some patients need a long-term disability pension at a young age [6, 7].

Work participation in SLE has received increasing attention in the past few years, and more recent data has become available on employment status, presenteeism (productivity loss while at work) and absenteeism (workdays lost due to sick leave) in workers with SLE. For example, the unemployment rate in this patient group is estimated between 34% to 62%, depending on the time point of assessment after diagnosis [3, 5, 8, 9]. Absenteeism and work disability are reported to be much higher compared with the general population [2, 3, 8–10]. Presenteeism and absenteeism are challenging to both patients and employers as patients feel more stressed if they are not able to perform their work at their best capacity. And for employers, it means cost increases and co-workers have to work extra to catch up with work for the employee that was absent.

Modifiable variables associated with reduced work participation should be identified to enable the development of intervention strategies to improve work participation in SLE patients in the future. This systematic review aimed to identify and summarize the results of all published longitudinal studies reporting on possible explanatory variables and predictors for work outcome in patients with SLE.

Methods

General methodology

A systematic review of the associations and predictors of work participation in patients with SLE was performed. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed where possible. The review protocol has been registered in PROSPERO (CRD42020161275). The data underlying this article will be shared on reasonable request to the corresponding author.

Terminology

The term work participation was used to encompass all definitions of work participation in paid work: from employment status to absenteeism (absence from work) and presenteeism (working while sick). For this review, included articles yielded the following definitions of

employment status: being employed (having work), being unemployed/health-related job cessation (not having work due to health problems), work loss (employed patients losing their work), work entry (unemployed patients starting work), work disability (having an impairment preventing having work) and unpaid work (performing work without reward). The used definitions of absenteeism were: sick leave (not working because of illness) and short-term disability (not working for a short time due to sickness), and for presenteeism: productivity loss (working but with less productive capacity) and work productivity impairment (having an impairment at work due to health problems resulting in less productivity at work).

Search strategy and eligibility

The search strategy was designed and performed by an experienced librarian (L.F.) and performed using MEDLINE, The Cochrane Library, Embase, CINAHL and PsycINFO from inception (1947) to July 2021. All relevant MeSH and free-text terms were used to represent the concepts of SLE and work participation. They included but were not limited to: ((Lupus Erythematosus, Systemic [MeSH] OR lupus erythematosus.tw OR SLE.tw) AND (Employment [MeSH] OR Absenteeism [MeSH] OR Presenteeism [MeSH] OR absent\$.tw OR absence.tw OR presenteeism.tw OR productivity.tw OR sick leave.tw)). Details on the search strategy are available in [Supplementary Data S1](#), available at *Rheumatology* online.

Studies eligible for inclusion in this systematic review needed to report longitudinal relations of explanatory variables [11, 12] on work participation outcome, e.g. absenteeism, presenteeism; and/or employment status. Explanatory variables encompass association results (an aetiological relationship between a risk factor and an outcome variable) and prediction results (a set of variables altogether predicting an outcome variable) [11, 12]. Articles should have reported data on patients with SLE aged ≥ 18 years. No language restrictions were applied.

Article selection and data extraction

According to the above-mentioned inclusion criteria, title and abstract screening were performed independently by two reviewers (B.S.B. and G.R.S.G.). Thereafter, the remaining potentially relevant articles were screened as full-text. Disagreement between both reviewers on the relevance of an article was discussed with a third reviewer (M.M.t.W.) until consensus was reached. Reference lists of the included articles were examined for additional relevant studies.

Data were extracted independently and simultaneously by two reviewers (B.S.B. and G.R.S.G.). Data was collected through a self-designed standardized form: (i) study information (e.g. study design, length of follow-up); (ii) data analyses (e.g. type of statistical analysis and confounders); (iii) baseline data (e.g. gender,

ethnicity, number of employed patients), disease characteristics (e.g. disease duration); and (iv) associations and/or predictors for work participation. Discrepancies in the data extraction between the two reviewers were discussed with the third reviewer (M.M.tW.) until consensus was reached.

Quality assessment of individual studies

The Quality in Prognosis Studies (QUIPS) tool was used to describe the quality of the individual studies [13]. The QUIPS tool includes an assessment of six domains (study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding and statistical analysis and reporting) to assess the risk of bias. The quality of the studies was evaluated independently by two reviewers (B.S.B. and M.M.tW.). Discrepancies regarding the judgement of the quality of the studies were discussed until consensus was reached.

Statistical analysis

A formal meta-analysis could not be performed as considerable heterogeneity was found between all included studies regarding applied outcome measures, applied statistical methods and instruments used to assess work participation. Narrative summaries are therefore used to present the data.

Results

Study selection

In total, 3106 records were identified through database screening and seven records through other sources (Fig. 1). After removing duplicates, 2420 articles remained for title and abstract screening. A total of 2332 records were excluded as these did not comply with the inclusion criteria, of which 829 records did not have work as an outcome measure, and 804 records were abstracts only. From the 88 articles that were read in full text, 73 records were excluded, of which 51 articles did not report on explanatory variables. Reference screening identified 20 additional articles that were excluded after full-text assessment as work was not an outcome measure ($n=3$), no full-text availability ($n=1$), no (adult) SLE patients included ($n=1$), or not reporting on explanatory variables ($n=15$). Eventually, 15 relevant studies were included in this review, reporting on longitudinal outcome measures and possible explanatory variables for work participation in patients with SLE [2, 4, 5, 10, 14–24]. Of these 15 studies, nine reported on associations [5, 10, 14–19, 24], four on predictors [4, 20, 21, 23], and two reported on both models [2, 22].

Outcome measures

Table 1 illustrates the outcome measures used in the association and prediction studies. The most frequently used outcome measure was employment status: either

being employed [2, 10, 14, 15, 17, 19, 22] or being unemployed [2, 5, 16–18, 22]. Absenteeism was used as an outcome measure in four studies [2, 10, 19, 24]. And presenteeism was reported as either productivity loss [18, 23] or having an impairment of productivity at work due to health problems [5, 10]. Definitions of work outcome measures used in the studies varied widely. For example, being employed was defined at different cut-off points for hours at work weekly [2] or duration of the same or temporary job [15, 17, 22], or being part of the workforce [19]. Other outcome measures on employment status were work disability [4, 19–21], unpaid work [10] and health-related job cessation [2].

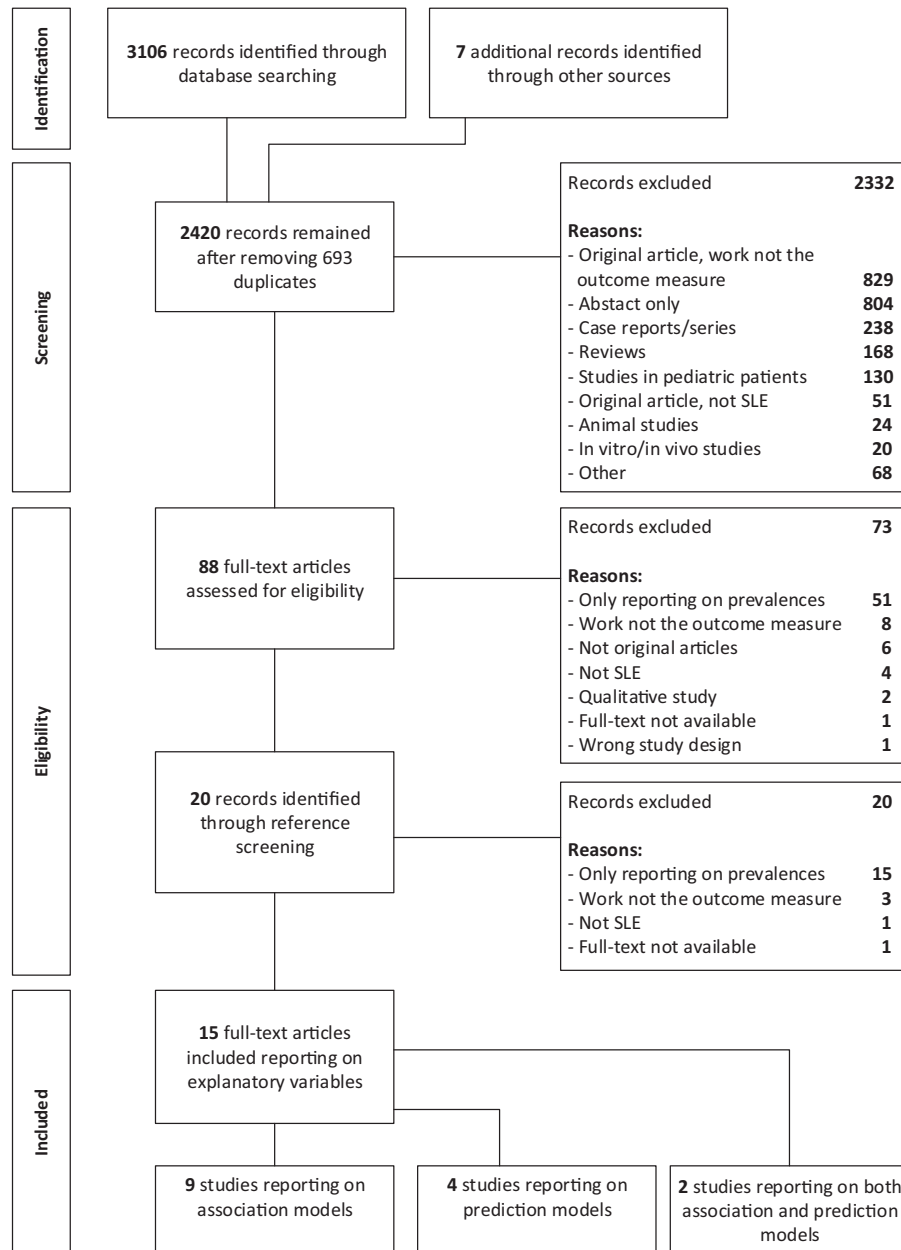
Studies reporting on variables associated with work participation

Detailed information on the included eleven studies regarding study design, study population, statistical methods and reported results for all outcome measures are shown in Supplementary Table S1, available at *Rheumatology* online. These articles reported results of studies in eight different patient cohorts and one registry. Nine studies were performed in the USA [2, 5, 10, 14–18, 24], one in Brazil [22] and one in Hong Kong [19]. No studies were performed in Europe or Africa. SLE was diagnosed using the ACR criteria [25, 26] in nine studies [2, 5, 14–19, 22]. Two studies used alternative classification of disease criteria: one was based on self-reporting [10], and in the other study, SLE was defined either by the International Classification of Disease (ICD) [24], or confirmed by a rheumatologist in combination with having at least two outpatient clinic visits of at least 30 days apart at the rheumatologist [24]. The majority of included patients were of Caucasian ethnicity except in one study, which included only patients of Chinese ethnicity [19]. Most studies included only patients of working age [5, 15–18, 22, 24]. Mean disease duration varied between 5 and 15 years. The duration of follow-up ranged between 6 months and >13 years.

Demographic variables

Associations between demographic variables and work participation were assessed in most studies, as presented in Table 2 [2, 5, 15–19]. Younger age was associated with lower odds for unfavourable employment status as an outcome, e.g. being unemployed, work loss, health-related job cessation or work disability [2, 16–19], but also showed some conflicting results. For example, one study using data from the Lupus Outcome Study (LOS) reported that younger age was significantly associated with being employed (age per year: OR 0.97, 95% CI [0.96, 0.98]) [15]. However, a second study using data from that same database (LOS) reported a non-significant association between higher age and health-related job cessation (OR 0.98, 95% CI [0.95, 1.0]) [2]. Another demographic variable frequently associated with work outcome in studies performed in the USA was ethnicity: work loss in patients of African-American ethnicity occurred more often compared with

Fig. 1 Flowchart



Flowchart presenting the identification and screening of articles, the articles assessed for eligibility and the final included articles.

Caucasian patients: $p < 0.001$ [5], and having a Caucasian ethnicity was associated with being employed: OR 0.72 (95% CI [0.56, 0.92]) [15].

Being higher educated was significantly associated with favorable employment status [2, 15, 18]. For example, having a college grade vs having no college grade was protective for health-related job cessation (OR 0.27, 95% CI [0.09, 0.84]) [2], and the completion of a bachelor's degree compared with no bachelor's degree was associated with being employed (OR 1.8, 95% CI [1.5, 2.2]) [15].

Disease variables

Associations between disease variables and work participation were assessed in nine out of eleven studies [2, 5, 10, 15–19, 24]. The impact of disease duration on work participation was investigated in four studies [16–19]. One study demonstrated longer disease duration to be associated with reduced work entry (only in the disease severity model, not in the final association model: OR 0.94, 95% CI [0.91, 0.97]) [17]. Another study performed in the same cohort reported that longer disease duration was associated with less work loss

TABLE 1 Overview of used outcome measures in association and prediction studies

Presenteeism		Absenteeism		Employment status	
Definition	Number of studies	Definition	Number of studies	Definition	Number of studies
Productivity loss	2 [18, 23]	Sick leave days	2 [2, 19]	Being employed	3 [14, 15, 22]
Mean h worked without impairment	1 [10]	Sick leave h	2 [10, 24]	Working h per day/week	2 [10, 19]
Work productivity impairment	1 [5]	Short-term disability h	1 [24]	Working 24 h per week or less	1 [2]
		Unable to work more than two months since diagnosis	1 [2]	Working <9 months per year	1 [2]
				Working 10+ h at baseline	1 [2]
				Newly employed	1 [2]
				Length of time until work entry	1 [17]
				Length of time until work loss	3 [16–18]
				Stop working	1 [2, 5]
				Unemployment after three years	1 [22]
				Work disability	4 [4, 19–21]
				Health-related job cessation	1 [2]
				Unpaid work	1 [10]

h: Hours.

among employed patients (full model: OR 0.93, 95% CI [0.91, 0.94]) [18]. The two remaining studies did not report an association between disease duration and work outcome [16, 19]. The study of Yelin *et al.* reported that higher disease activity, assessed using patient global assessment, was not associated with work loss among the employed (OR 1.06, 95% CI [0.96, 1.15]) [17]. In contrast, three other studies reported higher disease activity to be associated with an unfavourable work outcome (OR 1.1, 95% CI [1.02, 1.1], [16], OR 1.2, 95% CI [1.0, 1.4], [19], and $p < 0.0001$ [5]). The study of Lawson *et al.* reported a slightly decreased risk of being employed per unit increase in Systemic Lupus Activity Questionnaire (SLAQ) score: OR 0.98 (95% CI [0.97, 0.99] or being continuously employed (per unit increase in SLAQ score: OR 0.96, 95% CI [0.93, 0.98]) [15]. Depression [17], and some specific disease manifestations of SLE (joint disease/arthritis [2, 5], lung disease [2, 5], cognitive problems [5], and fatigue [5, 19]) were found to be associated with reduced work participation.

Work variables

Associations between work variables and work participation were assessed in six out of eleven studies [14–18, 22]. One study reported that job tenure per five years was significantly associated with a reduced risk of work loss (OR 0.8, 95% CI [0.7, 0.9]) [16], and shorter time since last regular work was associated with work entry (OR 0.73, 95% CI [0.62, 0.85]) [17]. High job demands combined with low job control was associated with increased work loss (OR 1.4, 95% CI [1.1, 1.7])

[18]. Higher level of physical functioning was associated with being employed (OR 1.03, 95% CI [1.03, 1.04]), continuous employment (OR 1.05, 95% CI [1.03, 1.07] [15]) and work entry (OR 1.02, 95% CI [1.01, 1.03] [17]). A lower level of physical functioning showed a small significant association with more work loss (OR 0.99, 95% CI [0.98, 1.00], $p < 0.05$) [17].

Studies reporting on predictors for work participation

Detailed information on the six included studies reporting predictors of work are shown in [Supplementary Table S2](#), available at *Rheumatology* online [2, 4, 20–23]. Outcome measures used in the six studies were work disability/health-related job cessation [2, 4, 20, 21], unemployment [22] and productivity loss [23]. Three studies were performed in the USA [2, 20, 21], two in Canada [4, 23] and one in Brazil [22]. The majority of included patients were of Caucasian ethnicity, except for one, in which predominantly patients of Hispanic or African-American ethnicity were included [20]. The mean age of included patients in most studies was of working age [2, 4, 20, 22, 23]. Follow-up duration varied between 12 months and 10 years.

Demographic variables

Demographic variables as predictors for work participation were assessed in four out of six studies [4, 20–22], of which education was most often assessed ($n=3$ studies) [4, 21, 22]. As shown in [Table 3](#), a higher educational level was the most frequently reported predictor

TABLE 2 Results of association studies reporting on demographic, disease and work-related variables associated with work participation in SLE

Presenteeism*			Favorable work outcome**			Unfavorable work outcome***		
Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]
Demographic variables								
			Younger age	Lower risk (n = 1) [15]	Age (continuous): β 0.97 [95%CI 0.96, 0.98] [15]	Younger age	Lower risk (n = 5) [2, 16–19]	Age 18–34 yrs vs 55–64 yrs: 0.4 [96%CI 0.3, 0.7] [16] Age (continuous): β 1.06 [95%CI 1.02, 1.11] [19] Age 18–34 yrs vs 55–64 yrs: 0.37 [95%CI 0.27, 0.75] [17] Age 18–34 yrs vs 55–64 yrs: 0.46 [95%CI 0.30, 0.69] [18] Age (continuous): β 0.98 [95%CI 0.95, 1.00] [2] African-Americans vs Caucasian: $p = 0.001$ [5]
			Caucasian ethnicity	Lower risk (n = 1) [15]	Non-Caucasian ethnicity vs Caucasian ethnicity: 0.72 [95%CI 0.56, 0.92] [15]	Caucasian ethnicity	Lower risk (n = 1) [5]	
			Higher educational level	Lower risk (n = 1) [15]	Completion of bachelor's degree vs no bachelor's degree: 1.8 [95%CI 1.5, 2.2] [15]	Higher educational level	Lower risk (n = 1) [18] Lower risk (n = 1) [2]	High school education or less vs more than college graduate: 3.8 [95%CI 2.4, 6.1] [18] College graduate vs non-college graduate: 0.27 [95%CI 0.09, 0.84] [2] Female vs male: 1.9 [95%CI 1.2, 3.0] [18] Never married vs married: 1.79 [95%CI 1.02, 3.14] [17]
						Male gender	Lower risk (n = 1) [18]	
						Never married	Higher risk (n = 1) [17]	
						Resident of North Carolina	Stable (n = 1) [2]	North Carolina vs South Carolina: 1.0 [95%CI 0.41, 2.4] [2]

(continued)

TABLE 2 Continued

Presenteeism*			Favorable work outcome**			Unfavorable work outcome***		
Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]
Disease variables#								
Moderate disease activity score	Higher risk (n = 1) [5]	Moderate (11–16) vs mild (0–10) SLAQ: $p < 0.0001$ [5]	Lower disease activity score	Lower risk (n = 2) [15–17, 19]	SLAQ (continuous): β 0.98 [95%CI 0.97, 0.99] [15] Patient global assessment (continuous): β 0.89 [95%CI 0.82, 0.98] [17]	Higher disease activity score in the preceding two years	Higher risk (n = 1) [19]	Mean SELENA-SLEDAI score in preceding 2 years (continuous): β 1.20 [95%CI 1.02, 1.42] [19]
Moderate fatigue score	Higher risk (n = 1) [5]	Moderate vs absent fatigue: $p = 0.015$ [5]	Diagnosed with cSLE vs aSLE	Higher risk (n = 1) [15]	cSLE vs aSLE: 0.62 [95%CI 0.42, 0.91] [15]	Longer disease duration	Lower risk (n = 1) [18]	Disease duration (continuous): β 0.93 [95%CI 0.91, 0.94] [18]
Severe fatigue score	Higher risk (n = 1) [5]	Severe vs absent fatigue: $p < 0.0001$ [5]	Diagnosed with SLE compared with controls	Higher risk (n = 1) [10]	SLE vs controls: $P < 0.001$ [10]	Depression	Higher risk (n = 1) [17]	CES-D (continuous): β 1.03 [95%CI 1.01, 1.05] [17]
Skin disease activity	Higher risk (n = 1) [5]	Skin disease activity (y/n): $p < 0.0001$ [5]	Dialysis	Higher risk (n = 1) [15]	Dialysis vs no dialysis: 0.74 [95%CI 0.56, 0.96] [15]	Thrombotic manifestations	Higher risk (n = 1) [16]	Thrombotic manifestations (y/n): 3.2 [95%CI 1.7, 5.9] [16]
Mild lung disease activity	Higher risk (n = 1) [5]	Mild vs no lung disease activity: $p = 0.029$ [5]	Fewer lung manifestations in past 5 years	Lower risk (n = 1) [17]	Lung manifestations in past 5 years (categorical): 0.45 [95%CI 0.20, 1.00] [17]	Severe musculoskeletal manifestations	Higher risk (n = 1) [16]	Severe musculoskeletal manifestations (y/n): 1.7 [95%CI 1.2, 2.5] [16]
Moderate lung disease activity	Higher risk (n = 1) [5]	Moderate vs no lung disease activity: $p < 0.0001$ [5]				Arthritis	Higher risk (n = 1) [2]	Arthritis (y/n): 3.3 [95%CI 1.2, 8.8] [2]
Severe lung disease activity	Higher risk (n = 1) [5]	Severe vs no lung disease activity: $p < 0.0001$ [5]				Pleuritis	Higher risk (n = 1) [2]	Pleuritis (y/n): 2.3 [1.1, 4.6] [2]
Mild stroke syndrome	Higher risk (n = 1) [5]	Mild vs no stroke syndrome: $p = 0.011$ [5]				Higher fatigue	Higher risk (n = 1) [19]	FACIT-F (continuous): β 1.06 [95%CI 1.01, 1.10] [19]
Moderate stroke syndrome	Higher risk (n = 1) [5]	Moderate vs no stroke syndrome: $p = 0.005$ [5]						
Severe stroke syndrome	Higher risk (n = 1) [5]	Severe vs no stroke syndrome: $p = 0.0005$ [5]						

(continued)

TABLE 2 Continued

Presenteeism*			Favorable work outcome**			Unfavorable work outcome***		
Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]
Moderate cognitive disease activity	Higher risk (n = 1) [5]	Moderate vs no cognitive disease activity: p = 0.0034 [5]						
Severe cognitive disease activity	Higher risk (n = 1) [5]	Severe vs no cognitive disease activity: p < 0.0001 [5]						
Mild muscle disease activity	Higher risk (n = 1) [5]	Mild vs no muscle disease activity: p = 0.054 [5]						
Moderate muscle disease activity	Higher risk (n = 1) [5]	Moderate vs no muscle disease activity: p < 0.0001 [5]						
Mild joint disease activity	Higher risk (n = 1) [5]	Mild vs no joint disease activity: p = 0.037 [5]						
Moderate joint disease activity	Higher risk (n = 1) [5]	Moderate vs no joint disease activity: p < 0.0001 [5]						
Severe joint disease activity	Higher risk (n = 1) [5]	Severe vs no joint disease activity: p < 0.0001 [5]						
Having SLE compared with controls	Higher risk (n = 1) [10, 24]	SLE vs controls: p < 0.001 [10] SLE vs controls: p < 0.01 [24]						
Work variables			Higher level of physical functioning	Lower risk (n = 2) [15–17, 19]	SF-36 physical functioning (continuous): 1.05 [1.03, 1.07] [15] SF-36 physical functioning scale (continuous): β 1.02 [95%CI 1.01, 1.03] [17]	Higher level of physical functioning	Lower risk (n = 1) [17]	SF-36 physical functioning scale (continuous): β 0.99 [95%CI 0.98, 1.00] [17]

(continued)

TABLE 2 Continued

Presenteeism*			Favorable work outcome**			Unfavorable work outcome***		
Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]	Independent variable	Result	OR [95% CI]
			Shorter time since last regular work	Lower risk ($n = 1$) [17]	Years since regular work (continuous): β 0.73 [95%CI 0.62, 0.85] [17]	More physical job demands	Higher risk ($n = 1$) [18]	Sum of physical job demands (continuous): β 1.06 [95%CI 1.0, 1.1] [18]
			Being employed after three years compared with baseline	Lower risk ($n = 1$) [22]	Being employed at follow-up compared with being employed at study entry: 2.25 [95%CI 1.4, 3.7] [22]	Higher cognitive functioning	Lower risk ($n = 1$) [17]	MOS cognitive functioning scale (continuous): β 0.98 [95%CI 0.97, 0.99]
			Currently employed at follow-up based on obesity status	Lower risk ($n = 1$) [14]	Currently employed at follow-up based on obesity status at baseline for non-obese vs obese patients: 0.5 [95%CI 0.3, 0.8] [14]	Job tenure per 5 years	Lower risk ($n = 1$) [16]	Job tenure per 5 years (continuous): β 0.9 [95%CI 0.7, 0.97] [16]
						High job demands and low control	Higher risk ($n = 1$) [18]	High job demands low control (y/n): 1.4 [95%CI 1.1, 1.7] [18]

The number of studies is indicated. All mentioned associations are statistically significant. In the case of multiple models per study, the outcome of the first model or most extensive model is shown. In the Online [Supplementary Table 1](#), available at *Rheumatology* online, the other outcomes can be found. The studies of Drenkard, Garris and Narayanan *et al.* did not show ORs; therefore p -values are shown. *Presenteeism work outcomes: work productivity impairment, work h missed due to SLE, work h missed for another reason. **Favorable work outcomes: being employed, being continuously employed, length of time until work loss at first specific SLE manifestation, h worked, work entry among unemployed. ***Unfavorable work outcomes: loss of days from the workforce and non-workforce activity, length of time until work loss, health-related job cessation, work loss, work disability over ten years after diagnosis, work loss among employed at diagnosis, work loss among employed. #Disease activity measured by Systemic Lupus Activity Questionnaire (SLAQ), patient global assessment and Safety of Estrogens in SLE National Assessment SLE Disease Activity Index (SELENA-SLEDAI). aSLE: adulthood-onset SLE; CES-D: Center for Epidemiologic Studies Depression Scale; cSLE: childhood-onset SLE; FACIT-F: Functional Assessment of Chronic Illness Therapy Fatigue; MOS: Medical Outcomes Study; OR: odds ratio; SF36: Short Form 36; SLAQ: Systemic Lupus Activity Questionnaire.

TABLE 3 Result of prediction studies reporting on demographic, disease and work-related variables predicting work participation in SLE

Work outcomes*			Unfavorable work outcome		
Predictor	Result	Coefficient (s.e.)	Predictor	Result	OR [95% CI]
Demographic variables					
			Younger age	Lower risk (n = 1) [20]	Age (continuous): β 1.1 [95% CI 1.02, 1.12] [20]
			Male gender	Higher risk (n = 1) [20]	Male vs female: 4.5 [95% CI 1.3, 15.9] [20]
			Poverty	Higher risk (n = 1) [20]	Poverty vs no poverty: 2.9 [95% CI 1.2, 7.0] [20]
			Higher education- al level	Lower risk (n = 3) [4, 21, 22]	Finished high school vs more than high school: 0.39 [95%CI 0.21, 0.7] [4] High school education or less vs beyond high school: 3.9 [95%CI 1.9, 8.2] [21] Education (continuous): β 0.09 [95%CI 0.01, 0.4] [22]
Disease variables					
Higher pain score	Higher risk n = 1 [23]	Pain score (con- tinuous): β 0.16 (0.06) [23]	Higher disease activity at diagnosis	Stable risk (n = 1) [4]	First SLEDAI-2K score (continuous): β 1.04 [95%CI 1.00, 1.08] [4]
			Higher disease activity during the study	Higher risk (n = 1) [20]	SLAM-R average (con- tinuous): β 1.3 [95%CI 1.1, 1.4] [20]
			Longer total dis- ease duration	Higher risk (n = 1) [20]	Total disease duration (continuous): β 1.2 [95%CI 1.1, 1.4] [20]
			Damage accrual	Higher risk (n = 1) [20]	SDI at last visit (con- tinuous): β 1.4, [95%CI 1.1, 1.7] [20]
			Hypertension	Higher risk (n = 1) [4]	Hypertension vs no hypertension: 2.2 [95%CI 1.2, 4.3] [4]
			Fibromyalgia	Higher risk (n = 1) [4]	Fibromyalgia vs no fibromyalgia: 5.1 [95%CI 2.6, 10.0] [4]
			Depression	Higher risk (n = 1) [22]	BDI >10 (depression) vs BDI <10: 2.3 [95%CI 1.0, 5.2] [22]
			Pleuritis	Higher risk (n = 1) [2]	Significant, data were not presented [2]
			Moderate or high aCL titers	Higher risk (n = 1) [22]	Moderate or high aCL titers vs low aCL titers: 2.1 [95%CI 1.2, 4.9] [22]
			Impairment in complex attention	Higher risk (n = 1) [22]	Impairment in complex attention vs no im- pairment: 2.2 [95%CI 1.1, 3.8] [22]
			Impairment in memory	Higher risk (n = 1) [22]	Impairment in memory vs no impairment: 3.6 [95%CI 2.1, 6.4] [22]
			Impairment in ex- ecutive functions	Higher risk (n = 1) [22]	Impairment in execu- tive functions vs no impairment: 1.8 [95%CI 1.2, 7.3] [22]

(continued)

TABLE 3 Continued

Work outcomes*			Unfavorable work outcome		
Predictor	Result	Coefficient (s.e.)	Predictor	Result	OR [95% CI]
			Impairment in reasoning/ problem solving	Higher risk (<i>n</i> = 1) [22]	Impairment in reasoning/ problem solving vs no impairment: 1.9 [95%CI 1.4, 7.2] [22]
Work variables					
Lower level of physical functioning	Higher risk <i>n</i> = 1 [23]	Level of physical functioning (continuous): β 0.33 (0.09) [23]	Higher physical demands of the job	Higher risk (<i>n</i> = 1) [21]	Higher physical demands of the job (higher DOT level, continuous): β 2.8 [95%CI 1.4, 5.4] [21]
Lower level of psychological functioning	Higher risk <i>n</i> = 1 [23]	Level of psychological functioning (continuous): β 0.18 (0.08) [23]			

The number of studies is indicated. All mentioned predictors are statistically significant. Damage accrual by the Systemic Lupus International Collaborating Clinics Damage Index at the last visit. Depression measured by Beck Depression Inventory. Impairment in complex attention measured by Mini Mental State Examination. Impairment in memory measured by digit span forward, logical memory. Impairment in executive function measured by digit span backward, verbal phonemic fluency. Impairment in reasoning/problem solving measured by comprehension. Higher level of physical and psychological functioning measured by visual analogue scale (0–10). *Work status outcomes are work disability [1–3], unemployment [4] and health-related job cessation [2]. Presenteeism outcome is productivity loss [23]. aCL: anticardiolipin antibodies; BDI: Beck Depression Inventory; DOT: Dictionary of Occupational Titles; OR: odds ratio; SDI: Systemic Lupus International Collaborating Clinics Damage Index; SLAM (-R): Systemic Lupus Activity Measure (- Revised); SLEDAI-2k: SLE Disease Activity Index 2000.

for a favorable employment status as an outcome measure in three studies, including permanent work disability/health-related job cessation and unemployment in patients being employed previously [4, 21, 22]. Having graduated from high school was found to be protective for being ever work disabled (OR 0.39, 95% CI [0.21, 0.7]) [4], and high school education or less was strongly predictive for work disability (OR 3.9, 95% CI [1.9, 8.2], overall model $p \leq 0.0001$) [21]. Finally, fewer years of education predicted unemployment after three years (OR 0.13, 95% CI [0.01, 0.5]) [22].

Disease variables

Disease variables as predictors for work participation were assessed in all six studies [2, 4, 20–23], of which disease activity was most often used (*n* = 3 studies) [4, 20, 21]. Higher disease activity score at diagnosis showed an unclear effect on employment status as no studies showed a significant relationship between disease activity at diagnosis and work participation. The study of Al Dhanhani *et al.* reported that high disease activity score at diagnosis, assessed using SLE Disease Activity Index 2000 (SLEDAI-2K), was not a predictor for work disability (OR 1.0, 95% CI [1.0, 1.1]) [4]. In contrast, the study of Partridge *et al.* reported a non-significant slightly increased risk (OR 1.1, 95% CI [0.9, 1.2]) for work disability in patients with higher disease activity score at diagnosis, assessed using the Systemic Lupus Activity Measure (SLAM) score [21].

Work variables

Only two studies assessed work variables as possible predictors [21, 23]. A higher level of physical and psychological functioning predicted less presenteeism (coefficient 0.18, s.e. 0.08, $p = 0.0198$) [23], and higher physical job demands strongly predicted more work disability (OR 2.8, 95% CI [1.4, 5.4]) [21].

Assessments of risk of bias

In nearly all studies, the quality was assessed as moderate to poor, as assessed with the QUIPS tool (Table 4). A high risk of bias in the domain ‘study attrition’ was judged in all but one study [22], as these studies did not provide information on patients who dropped out of the study. The risk of bias was judged low in nine studies as clear definitions of outcomes were provided and methods and setting of outcome measures were valid and the same for all study participants [10, 14–18, 20, 21, 23]. Furthermore, the risk of bias due to confounding was judged high in most studies as no confounders were assessed [2, 4, 5, 14, 15, 17–19, 22, 24].

Discussion

This study is the first to systematically review explanatory variables for work participation in patients with SLE. The results of this review showed that being of younger age, having a Caucasian ethnicity, higher educational level, lower disease activity score, a shorter

TABLE 4 Results of risk of bias assessment using QUIPS

	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
Al Dhanhani, 2009	±	-	-	±	-	-
Appenzeller, 2009	±	±	-	±	-	-
Bertoli, 2006	+	-	±	+	NA	+
Campbell, 2009	±	-	±	-	-	±
Clarke, 1993	±	-	-	+	NA	±
Drenkard, 2014	+	-	±	-	-	+
Garris, 2013	-	-	-	+	-	±
Katz, 2011	-	-	-	+	-	±
Lawson, 2014	-	-	±	+	-	+
Mok, 2008	-	NA	+	-	-	-
Narayanan, 2013	±	NA	+	±	-	-
Partridge, 1997	-	-	+	+	NA	-
Yelin, 2007	-	-	-	+	-	-
Yelin, 2009	±	-	+	+	-	-
Yelin, 2012	-	-	+	+	+	+

- = high risk of bias; ± = moderate risk of bias; + = low risk of bias.

disease duration, absence of specific disease manifestations, higher levels of physical functioning, less physical job demands and higher levels of psychological/cognitive functioning were associated with or predicted favorable work participation levels. Older age, non-Caucasian ethnicity, female gender, never being married, poverty, lower educational level, higher disease activity score, longer disease duration, specific disease manifestations, lower levels of physical functioning, more physical job demands and low job control, less job tenure, and lower levels of cognitive functioning were associated with or predicted an unfavorable work outcome.

Demographic variables were most often assessed in the included studies in this review. For example, having a younger age protected against unfavorable work participation outcomes in association and prediction studies [2, 16–20]. This is in line with three published reviews on variables related to work productivity in patients with other rheumatic diseases [27–29]. Furthermore, patients diagnosed with SLE at a young age might adapt their choice of education and job type to fit the presence of their disease early in life. A recent study reported a high rate of work participation in adulthood among patients with juvenile-onset SLE [30]. Studies on the influence of gender on work participation in SLE revealed conflicting results. Being male was associated with a lower risk of work loss/health-related job cessation [2, 18], but was predictive for higher work disability rates [20]. This finding is remarkable as SLE predominantly affects females resulting in low numbers of males being included in the studies [31]. It is known that males with SLE tend to have a higher organ damage score [32], and, therefore, might experience work disability more frequently. Findings on education

levels are in accordance with results of studies in patients diagnosed with other rheumatic diseases [27–29]. A possible explanation might be that higher education jobs are more often white-collar jobs (more sedentary), which may be more flexible and easier to maintain than blue-collar jobs.

Five studies showed that high disease activity scores were associated with or predicted an unfavorable employment status from the included studies that assessed disease variables [5, 15, 17, 19, 20]. Better treatment of disease activity might therefore be a target to enhance work participation. Remarkably, the disease activity score at diagnosis was no predictor of work participation, underlining the importance of effective treatment to lower disease activity [4, 21]. Other disease variables associated with work participation were specific disease manifestations (lung disease [2, 5], cognitive problems [5, 22], depression [17, 22]) and disease duration. This finding seems in line with the literature, as having cognitive problems or depressions are known factors associated with increased work disability [33–35].

As advised by Outcome Measures in Rheumatoid Arthritis (OMERACT), contextual factors play an essential role in work participation, especially work-related factors as job demands [36]. These factors are modifiable, and could help maintain employment. Only eight studies included work variables in their analyses [14–18, 21–23]. These studies demonstrated that lower levels of autonomy (high job demands and low control) [18], physical functioning [15, 17, 23], less physical job demands [18, 21] and higher levels of psychological functioning/higher cognitive functioning [17, 23] were related with poorer work participation both in association and prediction studies, which is also found in studies in other rheumatic diseases [27–29].

Although a decade ago a systematic review on work disability in patients with SLE was published [37], we now were able to include eleven new longitudinal studies on work participation in SLE [2, 4, 5, 10, 14–17, 19, 22, 24]. Our systematic review comprises more studies including work-related factors and demonstrates that several work variables are associated with work participation. This finding supports the idea that future interventions focusing on changing the work environment should be further explored to improve work participation of patients with SLE [38]. Also, the challenge of individual countries having different work and healthcare systems that have an impact on work on itself should be taken into account in future studies.

This study has several limitations. First, the quality of the included studies was judged moderate-to-poor according to the QUIPS tool, limiting the strength of the evidence. Second, most of the included studies originated from the USA, while no studies from Europe and Africa could be included. The results of this review can therefore not be generalized to SLE patients around the world. Third, most odds ratios were small, and CIs were large, resulting in non-significant results. Fourth, the studies included in this review were difficult to compare due to the heterogeneity in the populations investigated, measurement instruments and outcome measures used. Heterogeneous outcome measures, as well as diverse use of included variables are a known problem in research on work participation in patients with other rheumatic diseases [37, 39–41]. To enhance the comparability between studies and increase the value of research, a EULAR task force on work participation published EULAR points to consider for designing, analysing and reporting of studies with work participation as an outcome, specifically for inflammatory arthritis [42]. To standardize demographic, disease and work outcome measures used in studies, it is desirable to define a core outcome set of variables [30]. We therefore recommend applying the EULAR points to consider also in SLE studies to enhance and improve the quality of studies.

At last, we propose a research agenda for future research, focusing on extensive studies investigating both predictors for work loss among employed patients and work entry among unemployed patients. In addition, exploring the influence of more flexible work options since the COVID-19 pandemic on work participation in SLE patients might be an interesting topic for future research. It might be beneficial for SLE patients if they have the option to work from home most days of the week to avoid or reduce commuting time, long days at the office and no flexible h. This may help researchers to explore modifiable variables in future intervention studies aiming to enhance work participation in patients with SLE.

Conclusion

In conclusion, despite the heterogeneity of the included studies, younger age, Caucasian ethnicity, lower

educational level, lower disease activity, shorter disease duration, absence of specific disease manifestations, higher levels of physical functioning, less physical job demands and higher levels of psychological/cognitive functioning were associated with or predicted work participation. We recommend applying the EULAR points to consider for designing, analysing and reporting of studies with work participation as an outcome in inflammatory arthritis, as well as in SLE studies, to enhance the quality of studies and comparability between studies; to better understand the impact of SLE and treatment on work participation.

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Data availability statement

The data underlying this article are available in the article and in its online supplementary material.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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