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ORIGINAL ARTICLE

Burden of Systemic Lupus Erythematosus on Employment and Work Productivity: Data From a Large Cohort in the Southeastern United States

CRISTINA DRENKARD,[1] GAOBIN BAO,[1] GREG DENNIS,[2] HONG J. KAN,[3] PRITI M. JHINGRAN,[3] CHARLES T. MOLTA,[4] AND S. SAM LIM[1]

Objective. **To examine the burden of systemic lupus erythematosus (SLE) on work loss, unemployment, and work productivity impairment in an SLE cohort from the southeastern US.**

Methods. **We examined 689 SLE patients ages 18–64 years from the Georgians Organized Against Lupus (GOAL) cohort. GOAL is a longitudinal cohort predominantly derived from the Georgia Lupus Registry, a population-based registry established in metropolitan Atlanta. We used the Kaplan-Meier method to assess the proportion of patients who self-reported work loss since diagnosis. We compared unemployment between SLE patients and the general population from the same geographic area, calculating the standardized unemployment ratio (SUR) within demographic and disease strata. We also calculated the percentage of work productivity impairment by disease outcomes.**

Results. **Of 511 patients employed at diagnosis, 249 (49%) experienced work loss within an average disease duration of 13 years. The proportion of patients who lost their jobs since diagnosis was almost twice for African Americans than for whites. However, the SURs were similar across demographic characteristics, including race. Patients with severe disease activity and severe organ damage had the highest SUR at 4.4 and 5.6, respectively. Among those that remained employed, patients with severe fatigue, neurocognitive symptoms, and musculoskeletal symptoms had the highest impairment of work productivity.**

Conclusion. **SLE imposes a substantial toll on individuals and burden on society. Major factors that negatively impact work outcomes are fatigue, disease activity, and organ damage. More effective treatments along with coping strategies at the workplace are needed to reduce the burden of SLE on work outcomes.**

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic disease predominantly affecting young women at a time when many are establishing themselves in the workforce. With an unpredictable disease course often characterized by pain, fatigue, lupus flares, and progressive health decline, SLE can have a substantial impact on work outcomes. Studies from the US reveal that 15–40% of SLE patients are unemployed within 5 years of diagnosis (1–4). A longitudinal study among predominantly middle-class white women with SLE indicated that more than 60% were out of the workforce 20 years after the diagnosis (3).

Even if a lupus patient continues working, lupus flares, organ damage, or poor health can diminish productivity, contributing to the risk of permanent disability (1,5,6). In a multicenter study, 53% of patients changed duties within their job, 49% worked fewer hours per week, and 27% requested sick leave for >2 months at a time (4). A mean annual productivity cost of $8,659 was reported for SLE,

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[1]Cristina Drenkard, MD, PhD, Gaobin Bao, MPH, S. Sam Lim, MD, MPH: Emory University, Atlanta, Georgia; [2]Greg Dennis, MD (current address: Pharmaceutical Product Development, Rockville, Maryland): Human Genome Sciences, Medical Affairs, Rockville, Maryland; [3]Hong J. Kan, PhD, Priti M. Jhingran, PhD: GlaxoSmithKline, US Health Outcomes, Research Triangle Park, North Carolina; [4]Charles T. Molta, MD: GlaxoSmithKline, US Medical Affairs, Philadelphia, Pennsylvania.

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Address correspondence to Cristina Drenkard, MD, PhD, Division of Rheumatology, Emory University, School of Medicine, 49 Jesse Hill Junior Drive SE, Atlanta, GA 30303. E-mail: cdrenka@emory.edu.

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Significance & Innovations

- We examined the impact of systemic lupus erythematosus (SLE) on work outcomes in a large population-based SLE cohort in the southeastern US. By analyzing a representative sample of SLE patients that included a substantial number from disadvantaged sociodemographic subgroups, our findings advance the understanding of the complete burden of SLE on work outcomes.
- To our knowledge, this is the first population-based study in the US that reports the excess risk of unemployment in SLE compared with standards from the general population in the same geographic area, and further examines the burden of unemployment across demographic and disease severity subgroups.

and higher costs were associated with older age, greater disease activity, and worse health (7).

Most of the aforementioned findings arise from studies conducted with small or convenience samples that may not represent the full sociodemographic spectrum of people with SLE. The prevalence of SLE is 3–4 times higher in African Americans than whites, and disease onset occurs at a younger age among African Americans (8,9). Although SLE patients from minority groups are at high risk of poor disease outcomes and potentially more likely to lose their jobs, they have not been adequately represented in large US studies (3,7,10–12). Therefore, it is likely that the burden of SLE on work has been underestimated. Moreover, only a few studies in the US have compared work outcomes between SLE and the general population (2,7,10). As a result, it is difficult to determine how much effort and what type of intervention is necessary to improve work outcomes of high-risk SLE patients.

Taking advantage of a large population-based cohort of SLE patients with minority representation, we report the burden of SLE on work outcomes. We examined the proportion of work loss since diagnosis, the burden of unemployment compared to the general population, and the impact of disease activity and organ damage on work productivity impairment.

PATIENTS AND METHODS

The Georgians Organized Against Lupus (GOAL) cohort. The GOAL cohort encompasses a large sample of adult SLE patients from metropolitan Atlanta, Georgia. The overall aim of GOAL is to examine the impact of sociodemographic and health care factors on outcomes that are relevant to patients, health care providers, and policymakers. Recruitment and data collection methods, as well as the sociodemographic characteristics of SLE participants have been described previously (13). Briefly, the primary source of SLE enrollees is the Georgia Lupus Registry (GLR), a population-based registry designed to more accurately estimate the incidence and prevalence of SLE in Atlanta, an area with a large number of African Americans at high risk for SLE (8,14). Implemented through a partnership between the Georgia Department of Public Health (DPH) and Emory University, Emory investigators were enabled to collect protected health information from medical records without patient consent (under the Health Insurance Portability and Accountability Act Privacy Rule, 45 Code of Federal Regulations, parts 160 and 164). Furthermore, the Georgia DPH allowed Emory investigators to recruit GLR SLE patients into the GOAL Cohort.

More than 70% of GOAL participants were recruited from the GLR, and the remaining from lupus clinics at Grady Memorial Hospital (a large safety-net hospital in Atlanta) and Emory University, and from community rheumatologists in metropolitan Atlanta. By July 2012, 751 participants with a validated diagnosis of SLE completed the baseline survey. The survey, administered annually since August 2011, includes questions on sociodemographics, work status, and validated measures of disease outcomes. The Emory University Institutional Review Board, Grady Health System Research Oversight Committee, and the Georgia DPH Institutional Review Board approved the GOAL study protocol. All GOAL participants gave informed consent.

Patient selection. GOAL participants ages 18–64 years at the time of the baseline survey, who fulfilled either ≥4 of the 1997 updated American College of Rheumatology (ACR) classification criteria for SLE (15) or 3 ACR criteria with a final diagnosis of SLE by a board-certified rheumatologist, were examined in this study.

Measures and outcomes. *Work status.* We used an ad hoc questionnaire to measure self-reported work status at SLE diagnosis and baseline survey. The following categories were assessed: 1) working for pay (either full time or part time), 2) unemployed (not working for pay or disabled), and 3) student or homemaker.

Work loss. Work loss was measured as the proportion of SLE participants who were unemployed or disabled at survey completion out of those working for pay at disease diagnosis (Figure 1A). Participants who self-reported being a student or homemaker at survey completion were not counted to calculate the work loss rate.

Standardized unemployment ratio. To estimate the burden of SLE on unemployment as opposed to potential effects of sociodemographic or job market factors, we calculated the standardized unemployment ratio (SUR). GOAL participants ages 18–64 years who were unemployed or disabled were counted for "observed" unemployment in SLE (Figure 1B). We used unemployment estimates from the American Community Survey (ACS) to calculate the "expected" unemployment rates among individuals from the general population (16). ACS is a Census Bureau survey that collects data from samples of the US population. For geographic areas with populations larger than 65,000, the sample is sufficient to produce reliable

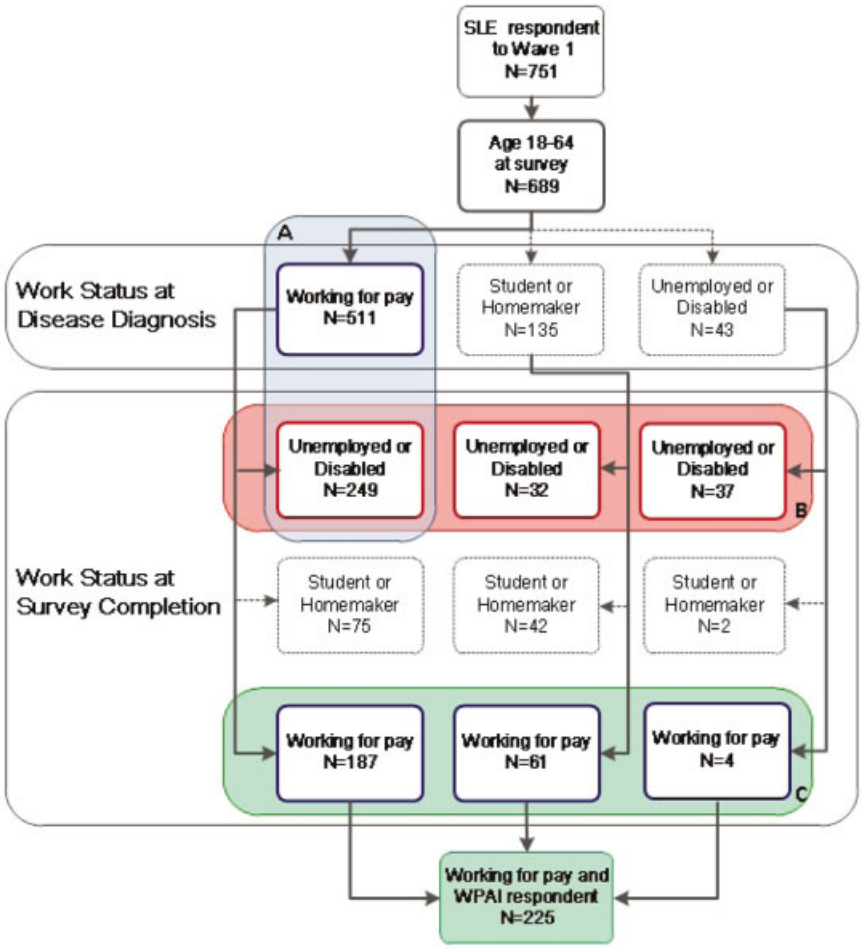


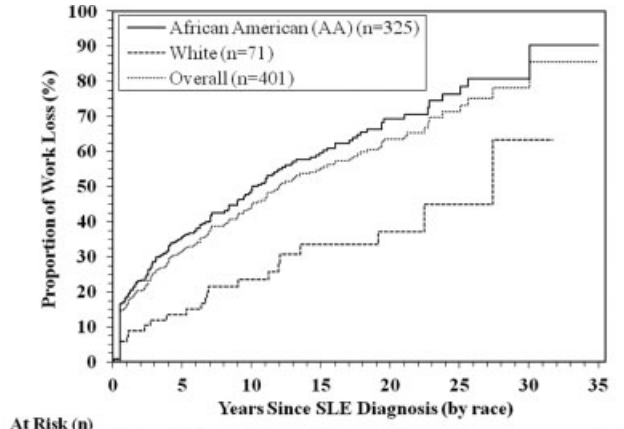
Figure 1. Schematic diagram of subsets of systemic lupus erythematosus (SLE) patients examined for work outcomes. **A,** (blue) subsets examined to calculate the work loss rate: proportion of participants who were unemployed or disabled at survey completion (n = 249) out of those who were working for pay at disease diagnosis (n = 511). **B,** (red) subsets examined to estimate the number of participants who were unemployed or disabled at survey completion (n = 318), which was used to calculate the standardized unemployment ratio. **C,** (green) subsets of participants who were working for pay at survey completion (n = 252) and were sent the Work Productivity and Activity Impairment Questionnaire (WPAI). Out of those, 225 respondents were examined for WPAI (green box). Dotted-line boxes represent subsets of SLE participants not eligible for corresponding outcome definitions.

estimates based on a year's worth of responses. We used ACS employment status (employed/unemployed) by demographics subgroups (age, sex, and race) from 2011 ACS samples of residents ages 18–64 years drawn from the same geographic area as GOAL participants (approximate adult population: 2,600,000 residents).

Work productivity impairment. We measured the overall work productivity impairment (WPI) due to health with the Work Productivity and Activity Impairment (WPAI) questionnaire (17). The WPAI is a validated tool applicable to a broad range of occupations and diseases (18). We applied the equation by Reilly et al (19) to calculate the WPI among SLE participants who were working for pay when surveyed (Figure 1C). The WPI accounts for the proportion of absenteeism and/or impairment of productivity at work due to a participant's health and her/his ability to work during the past week. WPI is expressed as percentage, with higher numbers indicating greater impairment and less productivity.

Disease activity. Disease activity was measured using the Systemic Lupus Activity Questionnaire (SLAQ), a validated survey with a recall period of 3 months and a score range of 0–44 (20,21). Higher scores indicate greater degree of self-reported disease activity. Additionally, items are weighted by organ system, similarly to the physician-rated Systemic Lupus Activity Measure. The SLAQ strongly correlates with physician-rated disease activity (20) and has excellent external reliability (r = 0.87) (21).

Organ damage. We measured patient-reported damage with a self-administered version of the Brief Index of Lupus Damage (BILD) (22). A recent validation of the self-administered BILD questionnaire in our GOAL cohort in-



At Risk (n)								
Overall	401	244	164	85	44	15	3	1
AA	325	186	123	60	28	11	2	1
White	71	54	38	23	15	4	1	0
Work Loss (%)								
Overall	0	32	44	55	63	71	78	85
AA	0	36	49	60	69	76	81	90
White	0	14	23	33	37	45	63	-

Figure 2. Work loss in systemic lupus erythematosus (SLE) by race. Out of 511 SLE cases that were working at disease diagnosis, 214 reported the year of work cessation. Those 214 patients were analyzed along with 187 that self-reported being employed at the time of survey. Seventy-five cases that reported being either student or homemaker were not included in the Kaplan-Meier analysis. The table displays the cumulative percentage of work loss by race at each time point. The difference in the proportion of work loss between African American and white patients was statistically significant ($P < 0.001$) by log rank test.

dicated excellent criterion validity for 80% of items and excellent test–retest correlation (r = 0.92) (23).

Statistical analysis. We calculated the proportion and 95% confidence interval (95% CI) (24) of SLE participants who lost their jobs after the diagnosis. Within the same set of participants, we used the Kaplan-Meier method (25) to estimate work loss since diagnosis (Figure 2). We used the work status category "being unemployed or disabled" (yes/no) as a surrogate of work loss. Therefore, for each participant who was employed at diagnosis and unemployed or disabled at survey completion, we estimated the period between the year of diagnosis and the most recent year when the individual became unemployed. Participants who were employed at both diagnosis and survey completion were censored. Log rank test was used to compare work loss by race.

The indirect method was used to calculate the ratio of the observed number of SLE patients unemployed at survey completion to the expected number of unemployed in the general population for the year 2011 (26). The age-standardized unemployment ratio was calculated separately for sex and race strata. The SUR was also calculated for SLE categories of disease duration, disease activity, and organ damage, adjusted by age, sex, and race.

We performed univariable (one-way analysis of variance; data not shown) and multivariable analyses using SAS PROC GENMOD to examine whether organ damage and disease activity were independently associated with WPI. GOAL participants who were working and responded to the WPAI questionnaire were analyzed (Figure 1C). The multivariable results were summarized within each category of the predictor variables as adjusted means (95% CI) by age, race, sex, education, and disease duration.

RESULTS

As shown in Figure 1, we examined 689 SLE participants ages 18–64 years among 751 GOAL survey respondents. Figures 1A, B, and C indicate the subsets of GOAL participants examined for each of the 3 study outcomes: work loss rate, SUR, and work productivity impairment, respectively.

Table 1 shows that 94% of the overall sample were women, 79.2% African American, 18.6% white, and 2.2% other races. The mean ± SD for overall disease duration and education was 13.1 ± 8.7 years and 14.2 ± 2.8 years, respectively. There were 252 participants working and 318 unemployed at the time of the survey. Age and disease duration were similar between employed and unemployed participants (age 42.9 and 44.6 years and disease duration 13.1 and 13.2 years, respectively). The working group had more whites (27.4%) and fewer African Americans (71.4%) than the unemployed group (9.4% whites and 89.0% African Americans, respectively). The proportion of patients who achieved some college or higher educational attainment, and those who were married or living with a partner was significantly larger for the working than the unemployed group (75.4% and 42.5% versus 54.7% and 24.8%, respectively). Approximately 70% of unemployed participants had federal insurance and 22.3% were uninsured, compared to 13.1% and 17.5% of those in the working group, respectively. Approximately 80% of unemployed participants reported an annual household below $30,000 compared to 34.6% among those in the workforce. The proportion of patients with severe disease activity and severe organ damage was 34.9% and 19.4% in the working group, respectively, as opposed to 66% and 44.7%, respectively, among those unemployed.

Among 511 participants who were working at disease diagnosis, 249 (49%) were unemployed at survey completion. Within an average of 13 years of disease duration, only 187 (37%) of SLE patients were still in the workforce. Of the 249 cases who had lost their job after the diagnosis of SLE, 214 provided the year when they stopped working. No significant differences of sociodemographic factors, disease duration, or disease outcomes were found between participants who did or did not provide the year of unemployment. The proportion of unemployed patients within 5 years since diagnosis was 32% (95% CI 27–37) (Figure 2). The proportion or work loss was significantly higher for African Americans than for whites ($P < 0.0001$). At 5 and 10 years since the diagnosis, 36% (95% CI 31–41) and 49% (95% CI 43–55) of African Americans stopped working compared to 14% (95% CI 7–24) and 23% (95% CI 15–36) of whites, respectively. The proportion of work loss among African Americans reached 81% at 30 years of disease, whereas few whites were unemployed after 15 years.

The SURs for demographic categories and disease-

Table 1. Sociodemographics and disease outcomes of systemic lupus erythematosus participants by work status at wave 1 survey completion*

Characteristic	All (n = 689)	Work status			P†
		Student/homemaker (n = 119)	Working for pay (n = 252)	Unemployed/disabled (n = 318)	
Sex					
Men	42 (6.1)	8 (6.7)	11 (4.4)	23 (7.2)	0.15
Women	647 (93.9)	111 (93.3)	241 (95.6)	295 (92.8)	
Race					
African American	546 (79.2)	83 (69.8)	180 (71.4)	283 (89.0)	< 0.0001
White	128 (18.6)	29 (24.4)	69 (27.4)	30 (9.4)	
Other	15 (2.2)	7 (5.9)	3 (1.2)	5 (1.6)	
Age at survey, years	43.8 ± 11.7	43.4 ± 14.4	42.9 ± 10.6	44.6 ± 11.3	0.069
Age at diagnosis, years	30.7 ± 11.0	30.7 ± 13.4	29.8 ± 10.6	31.5 ± 10.3	0.067
Disease duration, years	13.1 ± 8.7	12.9 ± 9.7	13.1 ± 7.8	13.2 ± 9.0	0.88
Education, years	14.2 ± 2.8	14.3 ± 2.6	15.3 ± 3.2	13.3 ± 2.2	< 0.0001
Educational attainment					
High school or lower	239 (34.7)	33 (27.7)	62 (24.6)	144 (45.3)	< 0.0001
Some college	225 (32.7)	48 (40.3)	59 (23.4)	118 (37.1)	
College or higher	225 (32.7)	38 (31.9)	131 (52.0)	56 (17.6)	
Marital status					
Married/cohabitated	233 (33.8)	47 (39.5)	107 (42.5)	79 (24.8)	< 0.0001
All other	456 (66.2)	72 (60.5)	145 (57.5)	239 (75.2)	
Insurance status					
Uninsured	136 (19.7)	21 (17.6)	44 (17.5)	71 (22.3)	< 0.0001
Private insurance	251 (36.4)	50 (42.0)	175 (69.4)	26 (8.1)	
Medicare/Medicaid	302 (43.8)	48 (40.3)	33 (13.1)	221 (69.5)	
Annual household income					
$0–$29,999	401 (60.0)	72 (63.2)	85 (34.6)	244 (79.2)	< 0.0001
$30,000–$49,999	102 (15.3)	13 (11.4)	49 (19.9)	40 (13.0)	
≥$50,000	165 (24.7)	29 (25.4)	112 (45.5)	24 (7.8)	
Disease activity score					
Mild (0–10)	185 (26.9)	42 (35.3)	88 (34.9)	55 (17.3)	< 0.0001
Moderate (11–16)	150 (21.8)	21 (17.6)	76 (30.2)	53 (16.7)	
Severe (≥17)	354 (51.4)	56 (47.1)	88 (34.9)	210 (66.0)	
Organ damage score					
No damage	193 (28.0)	35 (29.4)	105 (41.7)	53 (16.7)	< 0.0001
Mild (1–2)	262 (38.0)	41 (34.5)	98 (38.9)	123 (38.7)	
Severe (≥3)	234 (34.0)	43 (36.1)	49 (19.4)	142 (44.7)	

* Values are the mean ± SD or the number (percentage).
† Working for pay vs. unemployed or disabled.

related factors are displayed in Table 2. The SUR was above 3.4 for the overall SLE sample and across SLE demographic subgroups. The estimated ratio of unemployment was higher for men (SUR 4.6; 95% CI 3.1–6.9) than for women (SUR 3.5; 95% CI 3.1–3.9). African American patients were 3.5 (95% CI 3.2–4.0)–fold times more likely to be unemployed than their counterparts in the general population, and whites had an SUR of 3.8 (95% CI 2.6–5.4). Because the majority of patients in the cohort were women, we then examined unemployment by race within women. Unemployment for African American and white women was 3.4 (95% CI 3.0–3.9) times and 4.3 (95% CI 3.0–6.1) times higher, respectively, than for their counterparts in the general population.

In terms of disease-related factors, the risk of unemployment for patients with mild, moderate, and severe disease activity was 2.6 (95% CI 2.0–3.4), 2.8 (95% CI 2.1–3.7), and 4.4 (95% CI 3.8–5.0) times higher, respectively, than for individuals from the general population of similar age, race, and sex. SLE patients with an organ damage score ≥4 had the highest SUR (5.6; 95% CI 4.6–6.8). No substantial differences were observed between SUR within SLE patients by disease duration categories.

Among 252 participants working at survey completion, 225 responded to the WPAI questionnaire. Sociodemographic factors, disease duration, or disease status were comparable between respondents and nonrespondents (data not shown). SLE patients with severe disease activity reported approximately 50% of WPI, compared to 15% among those with mild activity (Table 3). Greater disease activity was associated with increasing WPI ($P < 0.0001$ for linear trend). Across all organ systems, WPI was significantly higher among participants with moderate or severe disease activity, compared to those with mild activity. Patients with severe symptoms of fatigue, forgetfulness or depression, muscle pain or weakness, joint pain, stiffness, or swelling, and those who reported strokes had the highest impairment of work productivity (above 50% WPI). No

Table 2. Standardized unemployment ratios (SURs) for SLE*

Category	SLE cases†	Unemployment		SUR (95% CI)‡
		Observed (SLE)	Expected (GP)	
Overall	570	318	88	3.61 (3.24–4.03)
Demographics				
Men	34	23	5	4.60 (3.06–6.92)
Women	536	295	84	3.51 (3.13–3.94)
African American	463	283	80	3.54 (3.15–3.97)
White	99	30	8	3.75 (2.62–5.36)
African American women	434	260	76	3.42 (3.03–3.86)
White women	94	30	7	4.29 (3.00–6.13)
Disease-related factors				
Disease duration, years				
0–5	101	59	17	3.47 (2.69–4.48)
6–15	235	123	36	3.42 (2.86–4.08)
>15	182	98	26	3.77 (3.09–4.59)
Disease activity score				
Mild (0–10)	143	55	21	2.62 (2.01–3.41)
Moderate (11–16)	129	53	19	2.79 (2.13–3.65)
Severe (≥17)	298	210	48	4.38 (3.82–5.01)
Organ damage score				
None (0)	158	53	24	2.21 (1.69–2.89)
Mild (1–3)	288	165	46	3.59 (3.08–4.18)
Severe (≥4)	124	100	18	5.56 (4.57–6.76)

* Values are the number unless indicated otherwise. SLE = systemic lupus erythematosus; GP = general population; 95% CI = 95% confidence interval.
† All SLE patients working for pay or being employed/disabled at the time of wave 1 survey.
‡ SUR adjusted by age, sex, and race using employment status data from the 2011 American Community Survey.

significant difference in WPI was found associated to overall organ damage or to any specific organ damage domains.

DISCUSSION

We examined the burden of SLE on work in a large cohort that is representative of the racial distribution and socioeconomic spectrum of SLE in the southeastern US. Nearly half of patients who were working at disease diagnosis had lost their jobs within an average of 13 years, whereas only 37% were still in the workforce. The work loss rate found in the present study is in the upper range previously reported in the US (15–50%) (1–4). Unemployed patients were in their early 40s and almost 80% reported an annual household income below $30,000. Seventy percent of unemployed patients received medical care from the federal government and 22% were uninsured. In contrast, 65% of patients in the workforce reported an annual household income above $30,000, whereas only 13% had federal insurance. These findings underline the substantial individual and societal burden associated with unemployment in SLE.

Multiple factors can account for work loss in SLE. Some of them are directly related to the condition, such as disease activity, organ damage, arthritis, cognitive impairment, or thrombosis (2,4–6,10–12,27). Demographic factors associated with poor disease outcomes have been reported to impact work outcomes (1–6,10,11). For instance, lower educational attainment has been found to increase the risk of unemployment (2–4,11), which is consistent with general labor market trends (28). GOAL patients in the workforce reported higher educational attainment and were more likely to be married than their unemployed counterparts, suggesting that social support might protect against work loss in SLE. Although our study was not designed to respond to that question, findings from the LUpus in MInorities, NAture versus nurture study indicate that poor social support might precipitate work disability in some patients (1).

Data on the impact of race, age, and sex on work outcomes have been inconsistent and difficult to interpret (1,2,4,11,29). Underrepresentation of vulnerable groups or no formal comparisons with the general population can explain some of the prior discrepancies (1–4,10,11,29). We found that the cumulative proportion of patients who lost their jobs was double for African Americans than whites since diagnosis through more than 30 years. Although awareness of these racial differences is essential to prevent work disability in SLE, comparison with the general population is fundamental to account for the risk associated with the disease.

We minimized the confounding effects of job market variability and sociodemographic factors on employment by calculating the adjusted SUR with data from a sample of residents drawn from the same community as SLE patients. Because GOAL participants were surveyed during a period of economic recession, the unemployment rates of reference were estimated for the same year (2011). The risk

Table 3. Work productivity impairment in SLE as a function of disease activity and organ damage*

Variable	Cases, no.	Adjusted WPI, mean (95% CI)†	*P*
Disease activity score			
Mild (0–10; reference)	80	14.9 (3.8–26.0)	–
Moderate (11–16)	66	37.7 (27.6–47.9)	< 0.0001
Severe (≥17)	79	49.5 (38.6–60.4)	< 0.0001
Organ damage score			
None (reference)	98	33.6 (23.0–44.2)	–
Mild (1–2)	83	28.7 (18.5–38.9)	0.24
Severe (≥3)	44	39.8 (28.1–51.6)	0.22
Disease activity by organ system score			
Fatigue			
Absent (0; reference)	26	17.6 (3.2–32.0)	–
Mild (1)	58	20.0 (7.7–32.3)	0.73
Moderate (2)	89	33.0 (22.6–43.4)	0.015
Severe (3)	52	50.6 (38.7–62.5)	< 0.0001
Skin			
Absent (0; reference)	73	16.6 (4.9–28.3)	–
Present (1)	152	38.9 (28.7–49.1)	< 0.0001
Lung			
Absent (0; reference)	78	20.2 (8.5–31.9)	–
Mild (1)	79	30.4 (19.4–41.5)	0.029
Moderate (2)	45	45.0 (32.2–57.8)	< 0.0001
Severe (3)	23	49.5 (35.5–63.5)	< 0.0001
Stroke syndrome			
Absent (0; reference)	101	25.9 (14.8–36.9)	–
Mild (1)	57	38.5 (26.5–50.5)	0.011
Moderate (2)	48	40.3 (27.4–53.2)	0.005
Severe (3)	19	52.1 (35.5–68.8)	0.0005
Cognitive			
Absent (0; reference)	54	20.7 (8.5–33.0)	–
Mild (1)	71	29.9 (18.6–41.1)	0.078
Moderate (2)	69	36.2 (25.0–47.5)	0.0034
Severe (3)	31	56.8 (43.0–70.5)	< 0.0001
Muscle			
Absent (0; reference)	57	19.8 (7.8–31.8)	–
Mild (1)	71	29.5 (19.0–40.1)	0.054
Moderate (2)	61	42.4 (30.0–54.7)	< 0.0001
Severe (3)	36	56.2 (43.3–69.0)	< 0.0001
Joint			
Absent (0; reference)	37	16.6 (3.7–29.5)	–
Mild (1)	78	28.4 (17.5–39.3)	0.037
Moderate (2)	74	40.7 (29.2–52.1)	< 0.0001
Severe (3)	36	53.8 (40.6–66.9)	< 0.0001

* SLE = systemic lupus erythematosus; WPI = work productivity impairment; 95% CI = 95% confidence interval.
† WPI adjusted by age, race, educational attainment, and disease duration.

of unemployment was 3.6 times higher in SLE than the general population. For all SLE demographic subgroups, the risk was at least 3.4 times higher than expected. Although SURs for men and white women were the highest (4.6 and 4.3, respectively), the 95% CIs overlapped with contrasting categories. Therefore, our results suggest that no matter what demographic subgroup SLE patients belong to, the risk of unemployment is substantially higher than expected in the reference subpopulation. Not surprisingly, sicker SLE patients yielded the highest risk of unemployment. Severe disease activity raised the risk to 4.4 and severe organ damage to 5.6. The unemployment risk by disease duration ranged from 3.4 for cases with short and intermediate disease duration to 3.8 for those with disease longer than 15 years. SURs were adjusted by age, sex, and race; therefore, our results suggest that factors directly related to disease severity may have higher impact on work loss than demographic characteristics or disease duration.

Among SLE patients still in the workforce, disease activity had a striking impact on work productivity. We measured WPI by combining absenteeism and reduced productivity while working. Patients with moderate and severe lupus activity reported 50% and 38% WPI, respec-

tively, while those with mild/no activity only had 15% of WPI. WPIs reported by our SLE patients are within the range of European SLE samples (30). The main impact was among patients with neurocognitive involvement, fatigue, or musculoskeletal symptoms, who reported more than 50% of WPI. Our results support previous findings that underscored the impact of the central nervous system and musculoskeletal manifestations on work outcomes (2,12).

The highest burden was, however, related to fatigue. WPI in patients with severe fatigue was 51%, compared to 18% in those without fatigue. Notably, fatigue was also found to have a profound impact on WPI in a European SLE cohort, with 49% and 21% of WPI among those with and without fatigue, respectively (30). Fatigue is perceived by SLE patients as one of the most burdensome and recalcitrant symptoms (31). Hence, it is not surprising that fatigue has substantial impact on work productivity, potentially threatening employment sustainability (6,29,32). Obtaining financial assistance to afford medical care is cumbersome when the primary contributing factors to work disability are subjective manifestations (5,32). Consequently, workplace strategies to assist SLE patients with pervasive symptoms of fatigue or pain are necessary to prevent devastating consequences on both individuals and society.

There are major contributions of our study. First, this is the first study in the US that examined the burden of SLE on employment and work productivity in a cohort predominantly derived from a population-based registry. Therefore, the proportion of African American to white patients is similar to that described by epidemiologic studies with a large number of high-risk individuals for SLE (9,33,34). Likewise, our cohort encompasses the full sociodemographic spectrum of SLE. Second, to account for work loss attributable to the disease, unemployment estimates in SLE were adjusted to standards from a representative sample drawn from the same community. Because SLE patients were surveyed during the years 2011–2012, when the US unemployment rate was high, the reference sample was also taken for the year 2011. Third, we advanced the understanding on how the disease impacts work outcomes by quantifying the burden of disease manifestations on work productivity. Although previous studies indicated that disease activity and organ damage are associated with greater work loss and indirect costs, the magnitude of self-reported work productivity impairment associated with specific disease manifestations has not been examined before in the US.

Our study has some limitations. First, work loss was examined with a cross-sectional design, which does not allow the assessment of all work status changes since diagnosis. Additionally, GOAL is not a true incident cohort and patients with severe disease, who are known to be at highest risk of work loss, may not have been captured or participated in the survey. As a result, the cumulative work loss rate may be underestimated. Second, since date of diagnosis and date of work cessation were based on patient-reported data, we cannot exclude a potential recall bias. However, other studies using patient-reported dates have found similar unemployment rates over time (1,3,4). For instance, work loss rates at 15 and 20 years were similar between the Lupus Outcomes Study (LOS) cohort (51% and 63%, respectively) and the GOAL cohort (55% and 63%, respectively) despite the fundamental sociodemographic differences between both samples (3). Notably, work loss rates at 5 years were higher among GOAL (32%) than LOS (15%) participants, suggesting that the initial disease period, when the disease tends to be more severe, may be critical, particularly for SLE patients from sociodemographic disadvantaged groups (35,36). This view is supported by longitudinal data from Partridge et al, who found 40% of work disability at 3.4 years since diagnosis in an SLE sample that included 53% African Americans and 47% patients from low educational attainment (4).

Third, the survey did not ascertain for unemployment attribution that would enhance our understanding of the direct impact of the disease on work loss. However, comparing unemployment with local standards, we were able to determine the excess risk that can be attributed to SLE. Fourth, although we reported that the percentage of productivity decline in the past week was associated with disease factors, the WPAI does not capture sufficient information to comprehensively measure actual productivity losses. As a result, we could not estimate indirect costs associated with cumulative work productivity or with permanent work loss. Finally, although more than 70% of participants consented in GOAL were drawn from the GLR and the rest from community- and university-based practices, it is not a perfect picture of the true universe of people with SLE. However, the GOAL cohort and the GLR have similar sociodemographic characteristics (data not shown), suggesting that our data source is a good representation of prevalent SLE patients in the southeastern US.

In conclusion, the risk of unemployment for SLE patients is almost 4-fold higher than the general population. SLE imposes a substantial toll on individuals and society, i.e., nearly half of patients in their early 40s are out of the workforce and 70% of them have Medicare and/or Medicaid, compared to only 13% of those still employed. The most important factors that increase the risk of unemployment are severe disease activity and organ damage; therefore, effective treatments to better control disease activity and minimize damage are needed across all demographic groups.

Among SLE patients still in the workforce, disease activity also has a sizeable impact on work productivity, with severe fatigue, cognitive impairment, and musculoskeletal activity being the most burdensome manifestations. If the negative impact of SLE on work outcomes is to be reduced, patients should be afforded assistance to maintain their employment and maximize their productivity. Implementing supportive policies to effectively manage disabling symptoms in the workplace can contribute to minimizing the striking effect of SLE on work performance.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors

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REFERENCES

1. Bertoli AM, Fernandez M, Alarcon GS, Vila LM, Reveille JD. Systemic lupus erythematosus in a multiethnic US cohort LUMINA (XLI): factors predictive of self-reported work disability. Ann Rheum Dis 2007;66:12–7.
2. Campbell R Jr, Cooper GS, Gilkeson GS. The impact of systemic lupus erythematosus on employment. J Rheumatol 2009;36:2470–5.
3. Yelin E, Trupin L, Katz P, Criswell L, Yazdany J, Gillis J, et al. Work dynamics among persons with systemic lupus erythematosus. Arthritis Rheum 2007;57:56–63.
4. Partridge AJ, Karlson EW, Daltroy LH, Lew RA, Wright EA, Fossel AH, et al. Risk factors for early work disability in systemic lupus erythematosus: results from a multicenter study. Arthritis Rheum 1997;40:2199–206.
5. Scofield L, Reinlib L, Alarcon GS, Cooper GS. Employment and disability issues in systemic lupus erythematosus: a review. Arthritis Rheum 2008;59:1475–9.
6. Baker K, Pope J, Fortin P, Silverman E, Peschken C. Work disability in systemic lupus erythematosus is prevalent and associated with socio-demographic and disease related factors. Lupus 2009;18:1281–8.
7. Panopalis P, Yazdany J, Gillis JZ, Julian L, Trupin L, Hersh AO, et al. Health care costs and costs associated with changes in work productivity among persons with systemic lupus erythematosus. Arthritis Rheum 2008;59:1788–95.
8. Lim SS, Bayakly RA, Helmick CG, Gordon C, Easley K, Drenkard C. The incidence and prevalence of systemic lupus erythematosus, 2002–2004: the Georgia Lupus Registry. Arthritis Rheumatol 2014;66:357–68.
9. McCarty DJ, Manzi S, Medsger TA Jr, Ramsey-Goldman R, LaPorte RE, Kwoh CK. Incidence of systemic lupus erythematosus: race and gender differences. Arthritis Rheum 1995;38:1260–70.
10. Yelin E, Tonner C, Trupin L, Panopalis P, Yazdany J, Julian L, et al. Work loss and work entry among persons with systemic lupus erythematosus: comparisons with a national matched sample. Arthritis Rheum 2009;61:247–58.
11. Yelin E, Tonner C, Trupin L, Gansky SA, Julian L, Katz P, et al. Longitudinal study of the impact of incident organ manifestations and increased disease activity on work loss among persons with systemic lupus erythematosus. Arthritis Care Res (Hoboken) 2012;64:169–75.
12. Panopalis P, Julian L, Yazdany J, Gillis JZ, Trupin L, Hersh A, et al. Impact of memory impairment on employment status in persons with systemic lupus erythematosus. Arthritis Rheum 2007;57:1453–60.
13. Drenkard C, Rask KJ, Easley K, Bao G. Lim SS. Primary preventive services in patients with systemic lupus erythematosus: study from a population-based sample in Southeast US. Semin Arthritis Rheum 2013;43:209–16.
14. Lim SS, Drenkard C, McCune WJ, Helmick CG, Gordon C, Deguire P, et al. Population-based lupus registries: advancing our epidemiologic understanding. Arthritis Rheum 2009;61:1462–6.
15. Hochberg MC, for the Diagnostic and Therapeutic Criteria Committee of the American College of Rheumatology. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [letter]. Arthritis Rheum 1997;40:1725.
16. US Census Bureau. A compass for understanding and using American community survey data: what general data users need to know. In: US Department of Commerce, editor. Washington (DC): US Goverment Printing Office; 2008.
17. Zhang W, Bansback N, Boonen A, Young A, Singh A, Anis AH. Validity of the work productivity and activity impairment questionnaire: general health version in patients with rheumatoid arthritis. Arthritis Res Ther 2010;12:R177.
18. Tang K, Beaton DE, Boonen A, Gignac MA, Bombardier C. Measures of work disability and productivity: Rheumatoid Arthritis Specific Work Productivity Survey (WPS-RA), Workplace Activity Limitations Scale (WALS), Work Instability Scale for Rheumatoid Arthritis (RA-WIS), Work Limitations Questionnaire (WLQ), and Work Productivity and Activity Impairment Questionnaire (WPAI). Arthritis Care Res (Hoboken) 2011;Suppl 11:S337–49.
19. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics 1993;4:353–65.
20. Karlson EW, Daltroy LH, Rivest C, Ramsey-Goldman R, Wright EA, Partridge AJ, et al. Validation of a Systemic Lupus Activity Questionnaire (SLAQ) for population studies. Lupus 2003;12:280–6.
21. Yazdany J, Yelin EH, Panopalis P, Trupin L, Julian L, Katz PP. Validation of the systemic lupus erythematosus activity questionnaire in a large observational cohort. Arthritis Rheum 2008;59:136–43.
22. Yazdany J, Trupin L, Gansky SA, Dall'era M, Yelin EH, Criswell LA, et al. Brief index of lupus damage: a patient-reported measure of damage in systemic lupus erythematosus. Arthritis Care Res (Hoboken) 2011;63:1170–7.
23. Drenkard C, Yazdany J, Trupin L, Katz PP, Dunlop-Thomas C, Bao G, et al. Validity of a self-administered version of the Brief Index of Lupus Damage in a predominantly African American systemic lupus erythematosus cohort. Arthritis Care Res (Hoboken) 2014;66:888–96.
24. Wilson E. Probable inference, the law of succession, and statistical inference. J Am Stat Assoc 1927;22:209–12.
25. Kaplan E. Nonparametric estimation from incomplete observations. J Am Stat Soc 1958;53:457–81.
26. Szklo M, Nieto J. Stratification and adjustment: adjustment methods based on stratification. In: Szklo M, editor. Epidemiology: beyond the basics. Gaithersburg (MD): Aspen Publishers; 2000. p. 265–79.
27. Bertoli AM, Alarcon GS, McGwin G Jr, Fernandez M, Bastian HM, Fessler BJ, et al. Systemic lupus erythematosus in a multiethnic U.S. cohort (LUMINA) XXVII: factors predictive of a decline to low levels of disease activity. Lupus 2006;15:13–8.
28. Bureau of Labor Statistics. Earnings and unemployment rates by educational attainment. Employment Projections 2012. URL: http://www.bls.gov/emp/ep_table_001.htm.
29. Utset TO, Fink J, Doninger NA. Prevalence of neurocognitive dysfunction and other clinical manifestations in disabled patients with systemic lupus erythematosus. J Rheumatol 2006;33:531–8.
30. Gordon C, Isenberg D, Lerstrom K, Norton Y, Nikai E, Pushparajah DS, et al. The substantial burden of systemic lupus erythematosus on the productivity and careers of patients: a European patient-driven online survey. Rheumatology (Oxford) 2013;52:2292–301.
31. Moses N, Wiggers J, Nicholas C, Cockburn J. Prevalence and correlates of perceived unmet needs of people with systemic lupus erythematosus. Patient Educ Couns 2005;57:30–8.
32. Murphy NG, Koolvisoot A, Schumacher R Jr, von Feldt JM,

Callegari PE. Musculoskeletal features in systemic lupus erythematosus and their relationship with disability. J Clin Rheumatol 1998;4:238–45.
33. Hochberg MC. The incidence of systemic lupus erythematosus in Baltimore, Maryland, 1970–1977. Arthritis Rheum 1985;28:80–6.
34. Lim SS, Bayakly R, Gordon C, Helmick CG, Easley K, Bao G, et al. The Georgia Lupus Registry: the incidence and prevalence of systemic lupus erythematosus [abstract]. Arthritis Rheum 2011;63:S952.
35. Burgos PI, McGwin G Jr, Pons-Estel GJ, Reveille JD, Alarcon GS, Vila LM. US patients of Hispanic and African ancestry develop lupus nephritis early in the disease course: data from LUMINA, a multiethnic US cohort (LUMINA LXXIV). Ann Rheum DIS 2011;70:393–4.
36. Alarcon GS, Calvo-Alen J, McGwin G Jr, Uribe AG, Toloza SM, Roseman JM, et al. Systemic lupus erythematosus in a multiethnic cohort: LUMINA XXXV. Predictive factors of high disease activity over time. Ann Rheum Dis 2006;65:1168–74.