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Association of Specific Organ Damage and Work Loss in a Population Based Cohort of Systemic Lupus Erythematosus Patients

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By

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Bachelor of Science

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2008

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An abstract of

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Abstract

Association of Specific Organ Damage and Work Loss in a Population Based Cohort of Systemic Lupus Erythematosus Patients

By Matthew Agan

Background: Systemic lupus erythematosus (SLE) predominantly develops in younger age groups, when many are establishing themselves in the workforce. The development of a chronic, autoimmune condition during this period can have a devastating impact on employment. The objective of this study was to evaluate the association of specific types of organ system damage with work loss in population-based cohort of SLE patients.

Research Design and Methods: The source of data was from the 2011 to 2012 annual patient reported survey of the Georgians Organized Against Lupus (GOAL) Study, an ongoing population-based cohort of patients with validated SLE in Atlanta, GA assembled primarily from the Georgia Lupus Registry (GLR). The GLR was supported by the Centers for Disease Control and Prevention and designed to more accurately estimate the incidence and prevalence of SLE. GOAL Study participants were surveyed regarding employment status at the time of survey completion along with other demographic information. Organ damage was measured using the Brief Index of Lupus Damage. Disease activity was measured using the SLE Activity Questionnaire (SLAQ). Logistic regression analysis was used to measure the association between categories of organ damage and employment/disability.

Results: Multivariable logistic regression showed significant associations between work loss and three organ systems: cardiovascular (Adjusted POR 8.71, 95% CI 3.41-22.21), renal (Adjusted POR 6.29, 95% CI 2.09-18.93), and for those with low SLE disease activity, neuropsychiatric (Adjusted POR 9.96, 95% CI 2.72-36.49 for multiple imputation). A total of 463 SLE patients were surveyed with a mean age of 46.6 (SD 10.0), 13.5 (SD 8.6) years of disease, and 14.2 (SD 2.8) years of education; 93.2% were female, 79.5% were black and 14.4% white. 200 (42.9%) were working and 263 (57.1%) were unemployed or disabled and thus had experienced work loss.

Conclusions: In total, 56.8% of SLE patients were unemployed or disabled at the time of the survey. Organ damage from SLE has a profound association with work loss. In the multivariable model, cardiovascular and renal damage were independently associated with work loss, which is in agreement with prior studies. Disease activity (SLAQ) acted as a mediator for neuropsychiatric damage; in those with low disease activity, neuropsychiatric damage was independently associated with work loss.

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BACKGROUND

Introduction

Work disability and early unemployment can have a profound impact on an individual, depriving him or her of income, employment benefits, socialization with peers, and self-esteem benefits. Aside from the individual impact, societal losses include the years of productivity that are lost when workers in the prime productive years are forced to take time off or permanently leave the work force because of medical illness. A growing body of literature has noted a link between systemic lupus erythematous (SLE) and low rates of employment (1-6). A systemic review reported that among those with SLE, the prevalence of employment was estimated to be 46% (7). For comparison, the prevalence of employment in the current working-age population in the United States averaged 58.6% during 2012, which is less than the 62-64% employment prevalence that predominated in the decade prior to the onset of the 2007-2009 economic recession in the United States (8).

Systemic Lupus Erythematosus

SLE is a chronic inflammatory autoimmune disease characterized by a relapsing and remitting course (9). Exacerbations of disease activity, or flares, occur when a person experiences new signs and symptoms of inflammation, including skin rashes, photosensitivity, fatigue, fever, and arthritis. In addition to disease activity, organ damage may accrue as a result of the disease, affecting the kidneys, heart, lungs, vascular system, nervous system, and gastrointestinal system. Anti-inflammatory and immunosuppressive medications have the potential to modify disease course but have a wide range of

potential side effects with long-term use, including organ damage and medication-associated comorbidities (10).

Disparities in and distribution of Systemic Lupus Erythematosus

Health disparities refer to differences in the incidence, prevalence, burden of disease, and mortality among distinct populations. These populations may be defined by age, race/ethnicity, sex, sexual orientation, or other characteristics. SLE is associated with age, gender and race disparities in the incidence, prevalence, and health outcomes of the disease. The disease preferentially affects the young, women, and ethnic minorities (11).

African-American women in particular suffer from incidence rates two to three times greater than those of Caucasian women (12). Some of these differences in disease burden may also manifest in the natural history of SLE. For example, in the LUMINA study, which longitudinally observed a large multiethnic cohort, African Americans exhibited acute disease onset and renal involvement with greater frequency (13).

SLE has also been linked to socioeconomic disparities. Those individuals with low income, limited education, and limited access to medical care are at increased risk of developing SLE and having adverse health outcomes (11).

Thus, there exists a mix of disparities among groups defined by characteristics that may or may not be deemed biological. A growing body of literature has sought to determine the basis of these disparities, thereby sorting out the complex influences of genetic and environmental factors. Still, the root causes of the socioeconomic disparities, which seem to have increased over time, are as yet not fully determined (11).

Incidence and Prevalence of Systemic Lupus Erythematosus

Incidence rates of SLE range from approximately 1 to 10 per 100,000 person-years and prevalence ratios range approximately from 20-80 cases/100,000 persons, with some reports of up to 200 cases/100,000 for certain populations (12, 14, 15). The distribution and determinants of lupus are not fully understood. Consequently, the incidence and prevalence of lupus have not been completely determined. Estimates of the incidence and prevalence of SLE vary widely due to use of different methodologies among studies, including different case definitions, limited resources, varying demographic groups targeted in assessment, lack of reliability from data and diagnosis, and limited contact with those who are at risk due to lack of health care (16) . Although the incidence rate of SLE varies across populations, there is evidence to show that incidence increased in the decades spanning the 1950's - 1990's (17). Some or all of that increase could also be accounted by increased recognition of the disease and earlier diagnosis (15).

Damage in Systemic Lupus Erythematosus

Damage is another spectrum of SLE severity that, unlike activity, is not reversible over time. As a result of the disease, organ damage may accrue affecting the kidneys, heart, lungs, vascular system, nervous system, and gastrointestinal system. This damage may be recorded and scored using various damage scales which rely on physician or patient reporting of disease characteristics.

Survival in patients with SLE improved dramatically in the twentieth century, with 5-year survival increasing from 45% in the 1950's to approximately 90% in the 1990's (18). Thus, understanding what drives morbidity has become a focus of epidemiologic research. Disease severity has emerged as an important predictor of

outcomes in lupus. As organ damage from SLE accumulates, associated morbidities may become more significant and possibly irreversible. In addition to disease activity, cumulative damage due to SLE has emerged both as an important outcome and as a predictor of other outcomes. Damage predicts not only mortality in SLE (19, 20) but also a wide range of other outcomes, such as health-related quality of life (21), health care utilization (22), impairment of life activities (23), and work disability (2, 6, 24-27).

Organ damage and work loss in SLE

SLE frequently affects individuals in the prime productive working years. It is known that those with SLE have a lower prevalence of employment, often as a consequence of the morbidity brought on by the disease and treatment side effects (28-30). Work loss in SLE patients is considered to be multifactorial, influenced by factors such as age (2, 3), race/ethnicity (4, 31), educational level (3), the physical requirements of the job (3), duration of disease (2), severity of disease activity (1, 2), and organ damage (2).

The definition of work loss varies across the literature, ranging from self-reported unemployment to verified work disability in which the patient is confirmed to be receiving a pension (7, 30). Regardless, precision in the definition of work loss is presumed not to be a great obstacle to understanding factors that determine work loss (32), even if it decreases comparability of studies.

Damage to specific organ systems and its associations with employment and formal work disability have been a recent focus of research. While validated damage instruments are used to evaluate populations to provide an overall picture of organ

damage due to SLE, these same instruments also provide information on damage to specific organ systems.

Evidence indicates an association of specific organ damage with work loss, and there is some evidence that it plays a causative role. In particular, musculoskeletal, cardiovascular, renal, and pulmonary damage have been associated with work loss (6, 33). A large longitudinal study by Yelin et al. (6) found that those with incident thrombotic events, which would encompass cardiovascular damage, NP damage and peripheral vascular damage in the BILD, were significantly more likely to experience work loss (HR 3.2, 95% CI 1.7-3.9).

Neuropsychiatric (NP) organ damage is associated with work loss in other studies (25, 33-35). One cross-sectional study by Bultink et al. (25) of a Dutch case series of 147 patients with SLE concluded that unemployed patients with SLE were significantly more likely to have acquired NP damage.

In a study of a population-based cohort of 117 Swedish SLE patients by Jönsen et al. (36), work disability was more prevalent, with a relative risk of 4.0 (95% CI 2.06-6.96) for those with NP manifestations compared to the general population. For those SLE patients without NP manifestations, work disability was more prevalent but not significantly more prevalent, with a relative risk of 2.1 (95% CI 0.9-4.2) compared to the general population.

Neuropsychiatric Manifestations of Lupus

Neuropsychiatric manifestations of SLE are an important source of morbidity and mortality for this patient population (37). In one series of pediatric-onset SLE patients, lifetime prevalence of at least one NP manifestation was estimated to be 95% (38).

Overall, nineteen neuropsychiatric syndromes of SLE have been identified and described by the American College of Rheumatology (ACR) (39). Each syndrome has its own set of diagnostic criteria and may be considered to affect either the central nervous system (CNS) or peripheral nervous system (PNS). Syndromes that affect the CNS include the twelve following: aseptic meningitis, cerebrovascular disease, demyelinating syndrome, headache, movement disorder, myelopathy, seizure disorders, acute confusional state, anxiety disorder, cognitive dysfunction, mood disorder, and psychosis. Syndromes that affect the PNS include the seven following: Guillain Barré syndrome, autonomic neuropathy, mononeuropathy, myasthenia gravis, cranial neuropathy, plexopathy, and polyneuropathy.

All nineteen of these syndromes commonly occur in non-SLE patient populations. The ACR nomenclature system defines sets of exclusionary criteria for each of the 19 neuropsychiatric syndromes of SLE to identify cases in which SLE is clearly not the etiology of the condition. The ACR system also identifies conditions that are recognized as "associations." Under this identification, it is not possible to attribute a particular NP syndrome to SLE or to another etiology exclusively, so it is attributed to both. Understood in this system of definitions is the inherent difficulty in identifying the share of etiology of any neuropsychiatric syndrome for patients with multiple possible etiologies. Hampering the process is a lack of a consistent diagnostic gold standard, such that attribution must be determined on a case-by-case basis (40).

The BILD instrument used in this study, which measures damage from SLE using self-reported patient characteristics, overlaps several of the neuropsychiatric syndromes. BILD contains information on the syndromes of psychosis, seizure disorders, and

cerebrovascular disease. The instrument also inquires about paralysis due to transverse myelitis, which would correspond to the NP syndrome of myelopathy. Thus, all NP syndromes which are addressed by the BILD instrument are considered CNS manifestations of NP SLE. However, it must be noted that the information provided by the BILD instrument is not sufficient to meet any diagnostic criteria for any of the syndromes.

Evidence suggests that NP SLE syndromes occur commonly in patients with lupus, even if definitive attribution of the syndromes to SLE is difficult. Ainiala et al., in a study of a large Finnish population cohort(41), concluded that headache, mild cognitive impairment, anxiety, mild depression, and polyneuropathy without electrophysiologic confirmation had such a high prevalence in a healthy control population that these symptoms should not be considered primary NP manifestations of lupus. Hanly et al. (37), in a series of 111 SLE patients, found that up to 41% of NP events were attributed exclusively to an etiology other than SLE. Hanly et al.,(42) in a separate study of a large cohort of SLE patients, found that only a minority of NP "events" in the first year after diagnosis were able to be attributed to SLE. With a more stringent model, 19% of events were attributed to SLE, and with a less stringent model, 38% of events were attributed to SLE. Regardless of attribution, those with NP events experienced lower health related quality of life (HRQOL) scores and higher organ damage scores.

Missing Data and Multiple Imputation

Missing data occur often during research and may be present for a multitude of reasons. For patient-reported data, such as the data set used for this study, the list of reasons expands to include those that are a result of how the subjects interact with the

survey. For instance, the subject may not understand the question, not know the answer, or simply refuse to report the information.

Missing data may be classified into one of three distinct categories by its relationship to the remaining data in the data set. The first category, missing completely at random, includes missing data in which the probability of being missing has no relationship to data from any other known variables in the rest of the data set. The second category, missing at random, includes variables in which the probability of being missing may depend on other variables but *does not* depend on the unobserved value of that missing variable itself. For instance, if the height variable in a data set were to be missing at random, it could be the case that men were more likely to refuse to report their height, but it could not be the case that shorter individuals were more likely to refuse to report their height. The third and final category, not missing at random, includes those variables in which the probability of being missing *does* depend on the unobserved value of the missing variable(43).

Multiple methods are available to deal with missing data. Listwise deletion, the traditional approach, eliminates all data for any observation in which data for a covariate is missing (44). Besides the loss of precision associated with decreased power, there is potential for bias to be introduced when the data is not missing completely at random. If all unobserved missing values are missing complete at random, then the complete case dataset could be viewed as a representative sample of the overall data set and not introduce any bias.

Often, the reason for missingness is not known, and assumptions must be made. Methods for imputation, which attempt to substitute values for missing data using

information from the other variables, often make the assumption that missing data are missing at random (45). Methods that assume that data are missing not at random do exist but are used less commonly (46) and are outside the scope of this discussion.

Multiple imputation is a statistical technique in which missing data values are substituted with simulated covariance matrix values that act as placeholders (47, 48). After multiple simulations, calculated values for missing data are averaged to create one point value for each missing data value. Multiple imputation, in contrast to single imputation (e.g. substituting the mean value for all other observations for the missing value), incorporates an estimate of the precision of the technique into the logistic regression model. The standard error term includes the variance within each imputed data set as well as the variance between imputed data sets.

Thus, some variance will be due to statistical noise from the imputation procedure. Adding more imputations will decrease the amount of variance from this source, but adding more iterations consumes computer resources in large datasets. Unless a high percentage of observations for a particular variable contain missing information, only 3-10 imputations are needed, although it would be possible to do many more. As described by Rubin(47), an equation is available to provide the efficiency of completing a given number of imputations compared to an infinite number of imputations:

$$Relative\ Efficiency\ (RE) = \left(1 + \frac{\lambda}{m}\right)^{-1}$$

where λ=Fraction missing and m=number of imputations

Purpose of Thesis

Although there is a growing body of literature regarding the impact of SLE on employment, there is limited knowledge on the role of specific organ damage in those with SLE. Prior studies have noted an association between damage to specific organ systems and increases in work disability (6, 25-27) or impairment of life activities (23).

This study seeks to determine the association of damage to specific organ systems with unemployment or work disability in a cross-sectional analysis of a population-based cohort of SLE patients. The study attempted to answer the following research question - compared to those without specific organ system damage, is specific organ system damage associated with increased odds of work loss?

HYPOTHESIS

Examining a community-based cohort of patients with a verified diagnosis of systemic lupus erythematosus and including only individuals who were employed at the time of diagnosis, the investigators hypothesize that those with specific types of organ system damage have experienced higher levels of work loss than those without the corresponding types of organ system damage.

METHODS

Data Source

The data source is the 2011- 2012 annual patient-reported survey of the Georgians Organized Against Lupus (GOAL) Study, an ongoing population-based cohort of patients with SLE in Atlanta, Georgia assembled from the Georgia Lupus Registry (GLR). The GLR is supported by the Centers for Disease Control and Prevention and designed to more accurately estimate the incidence and prevalence of SLE (16). Patients involved in the GOAL study are verified to meet the American College of Rheumatology (ACR) criteria for the diagnosis of SLE (49). IRB approval was previously attained from the Emory University IRB, and an amendment to the existing protocol was attained for additional personnel.

Inclusion and Exclusion Criteria

The GOAL study included those with SLE age 18 and over in Atlanta, GA at the time of survey completion. Only those who completed surveys by June 6, 2012 and reported full- or part-time employment at the time of SLE diagnosis were eligible for inclusion. Of these participants, those who reported their employment status at the time of survey completion as homemaker, student, retired, or unemployed aged 65 years or

older were also excluded from analysis. The figure outlines the inclusion and exclusion criteria in the selection algorithm.

Measures

GOAL Study participants were surveyed regarding employment status at the time of survey completion along with other demographic information. The primary outcome for this study is employment status at the time of survey completion, which is a dichotomous outcome. Subjects were characterized by the presence or absence of work loss. Work loss is defined as the subject being unemployed or being enrolled in formal work disability at the time of the survey. Only those who reported that they were employed full or part-time at the time of diagnosis were included in analysis.

The main exposure variables of interest are the presence or absence of damage to specific organ systems as measured by the Brief Index of Lupus Damage (BILD). BILD measures cumulative damage accrued since the onset of SLE (50). The BILD includes 26 non-reversible items encompassing nine organ systems. Subjects with a BILD score ≥1 were considered to have accrued overall damage.

The BILD score, which is calculated from the responses to the patient questionnaire, measures the amount of cumulative damage due to SLE. Nine organ systems as well as the three additional domains identified may contribute to the calculated score. For this study, if damage to a particular organ system contributed ≥1 to the BILD score, then that organ system was considered to have accumulated clinically significant damage.

Organ damage by system, as measured by BILD, was categorized as follows: ocular, cardiovascular, renal, pulmonary, neuropsychiatric, gastrointestinal, skin,

musculoskeletal, and peripheral vascular. In addition to the nine organ systems listed above, BILD incorporates information on the following: premature gonadal failure, malignancy, and diabetes.

For each organ system, the presence of damage was ascertained from the BILD instrument, which examines specific kinds of non-reversible damage that may arise from SLE. The specific items for each organ system are as follows. Ocular damage refers to any history of "something wrong with the retina" because of lupus, as well as cataracts. Neuropsychiatric damage includes any history of psychotic episodes, seizures, medications to prevent seizures, strokes, and paralysis in the arms or legs that is not due to multiple sclerosis. Renal damage includes any history of kidney transplant or dialysis for six months or longer. Pulmonary damage refers to any history of pulmonary hypertension, fibrosis, or interstitial lung disease. Cardiovascular damage refers to any history of "coronary or heart bypass surgery," angina, congestive heart failure, a "heart attack" or myocardial infarction, and pericarditis lasting longer than six months. Peripheral vascular damage refers to "loss of flesh or thinning on the ends of" the fingers because of lupus, "loss of a finger, toe, or part of an arm or leg not due to an accident" but because of lupus, and deep venous thrombosis in any extremities. Gastrointestinal damage refers to any history of peritonitis lasting six months or longer, as well as abdominal surgery due to lupus including surgery involving the esophagus, stomach, small intestine, large intestine or colon, spleen, liver, pancreas, gall bladder, or any other part of the abdominal cavity. Musculoskeletal damage refers to any history of avascular necrosis, osteomyelitis, or any bone fracture that resulted from osteoporosis. Skin damage refers solely to any history of a skin ulcer that lasted at least six months.

Covariates included demographic, employment, behavioral, social, comorbidity, SLE, and health variables.

Demographic variables included age at the time of interview, sex, and race/ethnicity, marital status, and Body Mass Index (BMI). Age at the time of the interview was categorized into three groups: 18-34 years, 35-49 years, and ≥50 years. Sex was classified as a dichotomous variable with males as the reference group. Three ethnic/racial categories were included: non-Hispanic white, non-Hispanic African-American, and other (Asian, American Indian or Alaska Native, Native Hawaiian, Hispanic, and self-elected multiple races). Marital status was controlled as a categorical variable (never married, married, separated, divorced, and widowed). BMI was calculated as weight in kilograms divided by height in meters squared and was analyzed as a continuous variable.

Employment-related variables included years of education completed and pre-diagnosis physical demands of employment. Years of education was recorded as a discrete variable in which the subject reported the highest level of education attained, starting with first grade and continuing until a maximum of 23 years. Years of education was analyzed as a continuous variable without grouping into categories. Physical demand of pre-diagnosis employment was classified using the Dictionary of Occupational Titles (DOT) database (51, 52). The DOT assigns one of five strength levels (sedentary, light, medium, heavy, very heavy) to jobs based on the maximum weight lifted and duration of the weight being carried during the course of occupational activities. Subjects provided information on pre-diagnosis occupation, which was then matched to the database.

During analysis, three categories of strength classification were used: sedentary, light, and medium or greater. The sedentary category was used as a reference group.

SLE disease-related variables included age at SLE diagnosis, duration of SLE, and activity as measured by the SLE Activity Questionnaire (SLAQ) (53, 54). Age at SLE diagnosis in years, a continuous variable, was calculated as the time between the subject's date of birth and the date of SLE diagnosis. Duration of SLE in years, a continuous variable, was calculated as the time between date of SLE diagnosis and date of survey completion. The SLAQ, a questionnaire designed to determine the level of SLE disease activity in situations where physician assessments for clinical evaluations are not feasible, assesses 24 symptoms related to disease activity: weight loss, fatigue, fevers, oral ulcers, malar rash, photosensitivity, vasculitis, other rashes, alopecia, lymphadenopathy, dyspnea, chest pain, Raynaud's phenomenon, abdominal pain, paresthesias, seizures, stroke, memory loss, depression, headaches, myalgias, muscle weakness, arthralgia, and joint swelling. SLAQ is similar to the BILD in that it aggregates and weights patient-reported answers to survey questions to deliver a numerical score for one spectrum of SLE disease severity. Information from these 24 items in the SLAQ is assessed in a formula that delivers a score, 0 to 44, that may be used as measure of level of overall disease activity.

Comorbidities were analyzed as multiple dichotomous variables, classified as the presence or absence of the following eight items: emphysema, asthma, bronchitis, chronic obstructive pulmonary disease, depression, high blood pressure, and high cholesterol. Smoking status was categorized as current smoker, former smoker, or having never smoked.

Current medication use was analyzed as multiple dichotomous variables, characterized by the current use or non-use of the following medications: corticosteroids; hydroxychloroquine sulfate; methotrexate; cyclophosphamide; cyclosporine; mycophenolate mofetil; dapsone; azathioprine; belimumab; rituximab; any tumor necrosis factor inhibitor such as etanercept, adalimumab, or infliximab; any bisphosphonate such as alendronic acid or ibandronic acid; multivitamins; vitamin D supplements; calcium supplements; and daily aspirin. The survey did not include other additional medication information such as indication or dosage.

Statistical Analysis

A descriptive analysis of the data was compiled along with information on counts of missing for each variable. Subsequently, univariate logistic regression analysis was performed and the Wald chi-square test was used to determine which covariates were significantly different among those SLE patients that were currently employed versus those who had experienced work loss.

After assessment of interaction and confounding, multivariable logistic regression was performed to assess the relationship between the presence of specific organ damage and work loss. Multicollinearity was evaluated by calculating the variance inflation factor (VIF) of each candidate variable. A VIF<10 was considered acceptable.

Interaction was tested using the cross products of the exposure variables and the covariates that were assessed in logistic regression. Interaction terms were tested together in a "chunk test," a version of the likelihood ratio test (LRT) in which terms may be added or removed in groups (55). If the LRT yielded a non-significant p-value (>0.05), then backwards elimination (BWE) was performed to determine if any individual

interaction terms should remain in the model. Because of the large number of interaction terms tested in this manner, the adaptive Holm adjustment to the stepdown Bonferroni procedure was used to account for multiple hypothesis testing. The adaptive Holm adjustment to the stepdown Bonferroni procedure is less conservative than the traditional Bonferroni adjustment, allowing for more power while still controlling for the family-wise error rate (56, 57). If, as a result of both the chunk test and the BWE approach, no interaction terms were found to be significant at their respective adjusted p-values, then all interaction terms were removed. Any interaction terms with an adjusted p value <0.05 were retained.

The investigators built the multivariable regression model by beginning with a model that included all nine types of organ system damage. Adding and removing one variable at a time in a stepwise fashion, the change in the point estimates for the association between each type of damage and unemployment/work disability was then evaluated. The covariates that produced an OR estimate meaningfully different from the unadjusted OR (education, current comorbid depression, current comorbid high blood pressure, current corticosteroid use) were included in the subsequent multivariable model. At that point, the investigators re-inserted each of the previously eliminated covariates (BMI, age at time of interview, race, and gender marital status, physical requirements of occupation, smoking status, Age at time of SLE diagnosis, SLE duration, presence of comorbidities including emphysema, asthma, bronchitis, COPD, high cholesterol levels, stomach ulcers, “liver problems”, and “gall bladder problems”, medications including plaquenil, methotrexate, Cytoxan, cyclosporine, mycophenolate mofetil, dapsone, azathioprine, belimumab, rituximab, anti-TNF medications, osteoporosis medications,

multi-vitamins, vitamin D, and calcium) individually to evaluate whether their inclusion in the model produced a meaningful difference in the OR estimate. No other variables were added to the model because of this step.

For the multivariable logistic regression models, two strategies were employed to deal with missing data in the dataset. The first strategy, complete case analysis, handles missing data by deleting rows of data, with missing information for one or more variables. In complete case analysis, no attempt is made to impute, or fill in, the missing data values. Another method, multiple imputation, maximizes the amount of data that can be used in logistic regression models.

For the data set used in this study, five imputations were completed. Thus, relative efficiency of the imputation would range from approximately 91% with 50% missing information for the given variable to 98% with 10% missing information for the given variable.

Data analysis was performed using SAS 9.3 software. Hypothesis testing was 2-tailed. Adjustments for multiple comparisons were made only when testing interaction terms, and no other adjustments for multiple comparisons were made. For hypothesis testing, p-values <0.05 were considered to be significant.

RESULTS

Descriptive Statistics:

The cohort of validated systemic lupus erythematosus (SLE) cases who were employed full-time or part-time at diagnosis consisted of 463 patients. The cohort included in complete case analysis consisted of 430 patients. The racial distribution for the cohort was 79.7% African American, 14.3% White, and 6.1% multiracial/other races. Women comprised 93.3% of the sample. The mean educational achievement was 14.2 years. The mean age at the time of survey was 46.2 years old (standard deviation (SD) 10.0 years) and the average duration of disease is 13.5 years (SD 8.6 years). The mean age at diagnosis of SLE was 33.2 years old ± 9.2 years. The mean SLAQ score was 17.9, and the mean BILD score was 2.3. The most common comorbidity was high blood pressure (58.0%) followed by depression (38.1%) and then high cholesterol (16.6%). Of the 463 patients included in analysis 263 (56.8%) had the outcome of work loss. These data are shown in Table 1, which includes counts, percentages, and information on the number of missing observations for each covariate.

Univariate analysis:

In univariate logistic regression analysis, covariates significantly associated with increased work loss included many of the variables examined.

Disease-related variables that were significantly associated with increased levels of work loss include the following: higher disease activity as reported in SLAQ, overall organ damage as defined by BILD, all specific organ domains of damage as evaluated by the BILD except for pulmonary and skin (including ocular, NP, cardiovascular, musculoskeletal, peripheral vascular, gastrointestinal, and renal).

The demographic variables were associated with increased work loss were age category at time of interview and being divorced, separated, or widowed. Employment-related variables that were associated with increased work loss include greater occupational physical requirements as defined by the DOT for job held before SLE diagnosis. Comorbidities associated with higher work loss include the following: high cholesterol, high blood pressure, depression, stomach ulcers, "gall bladder problems", and diabetes. Medications associated with increased work loss include current corticosteroid treatment and osteoporosis medications. Covariates significantly associated with decreased work loss included white race and increasing education level.

Multivariable Logistic Regression Analysis:

Using a hierarchical backward elimination approach, there was evidence of interaction for NP damage and SLE disease activity (p=0.0009 unadjusted, p=0.045 after adaptive holm adjustment). Because of interaction with SLE disease activity, results for adjusted prevalence odds ratios for NP damage stratified on SLE disease activity are presented in tables 4 (complete case analysis) and 6 (multiple imputation). In patients with low disease activity, NP damage is significantly associated with work loss in both analyses (adjusted POR 8.74, 95% CI 2.14-35.71 for complete case analysis; adjusted POR 9.96, 95% CI 2.72-36.49 for multiple imputation).

Only those subjects with complete information for covariates in the multivariable model were included in complete case analysis. Of the 463 eligible individuals, 415 had complete information for all covariates present in the multivariable model. Results for complete case analysis are available in table 3, and results for the multiple imputation model are available in table 5. The models used are identical; only the method for

handling missing data was different. Disease-related variables that were significantly associated with increased levels of work loss include cardiovascular damage (Adjusted POR 9.43, 95% CI 3.46-25.71 for complete case analysis; Adjusted POR 8.71, 95% CI 3.41-22.21 for multiple imputation) and renal damage (Adjusted POR 6.29, 95% CI 2.05-19.28 for complete case analysis; Adjusted POR 6.29, 95% CI 2.09-18.93 for multiple imputation).

DISCUSSION

Lupus is a heterogeneous disease with manifestations across multiple organ systems. This study utilized a cross-sectional design to examine the association between specific domains of organ damage and work loss in a community-based cohort of SLE patients that was initially derived from a population-based lupus registry. The presence of cardiovascular damage, renal damage, and for those with low disease activity, neuropsychiatric damage were profoundly associated with work loss in this cohort, even after adjustment for confounders. Other types of organ damage (ocular, musculoskeletal, peripheral vascular, and gastrointestinal) were significantly associated with work loss in univariate analysis but not after adjustment for confounders. Skin and pulmonary damage were not significantly associated with work loss in univariate or multivariable logistic regression.

For the population studied, the average age of the group who experienced work loss was 46.4 (SD 10.3) years of age. Evidence suggests that patients with chronic diseases such as lupus have difficulty re-entering the workforce, so that those who exit may find that their careers end much earlier than the rest of the population (3, 58). Aside from the psychosocial benefits that gainful employment provides, the decreased years of employment may significantly decrease the wealth that the person is able to accumulate for savings and retirement (28, 29).

An interaction effect was present between SLE disease activity and NP damage, such that NP damage was independently and significantly associated with work loss only among those with low SLE disease activity. This result highlights the association of NP damage with those who may otherwise display signs of low disease severity. Future

studies can examine whether this effect modification is present for other NP manifestations that have shown associations with work loss, such as cognitive dysfunction.

It is possible that a healthy worker effect is present in this study, in which those with higher disease severity have a greater rate of mortality or displacement and do not enroll in the study. The study population of GOAL is derived from the population-based Georgia Lupus registry, which measured incidence of lupus in 2002-2004 and prevalence of lupus in 2002. In the time interval between collection of information for the registry and the synthesis and development of the GOAL study, individuals could have died or have moved away from the metro Atlanta area to live with family because of lack of resources, a likely scenario that could differentially affect those with the outcome of work loss. If mortality or displacement were to contribute to a healthy worker effect, it would likely lead to an underestimation of the effect of organ damage on work loss. This could account for lack of effect of disease duration that was observed, as another study that was completely population based did note an increase in work disability with increased disease duration (59).

Suggestions for interventions aimed at work disability in SLE populations have focused on prevention of early workforce exit (34, 35, 58). Neuropsychiatric damage poses a particular challenge, as these patients have a higher prevalence of cognitive dysfunction than others with SLE (60). Panopolis et al. (34), in an investigation of associations of neurocognitive deficits with work disability in a group of SLE patients, described a significant and independent association of memory impairment with work disability. Utset et al. (31) also describes an association of cognitive dysfunction as

measured by neurocognitive tests and work disability in a cohort of SLE patient. A third study by Appenzeller et al. (35) described an association between deficits in cognitive domains such as executive function and memory and work disability. All three authors suggest cognitive training and rehabilitation programs, which also have therapeutic applications in patients with multiple sclerosis who show cognitive dysfunction (61), as an option that could possibly allow these patients to prolong employment.

Strengths

One strength of this study is the source of the study population, which is comprised of validated SLE cases that were initially drawn from a large population-based registry. Many studies that have examined work loss in SLE consisted of relatively small sample sizes from single-center sites (58). The advantage of a cohort that is based on a population-based registry is that it more accurately represents the real world population (62) and is more generalizable to the wider population of patients with SLE. As the study population reflects the composition of the Georgia Lupus Registry, it includes a high proportion of African-Americans, who are at higher risk of developing SLE with severe complications.

Another strength of this study is that multiple imputation was utilized in an effort to be as efficient as possible in analysis of the data. Rather than analyzing only cases with complete information on covariates, multiple imputation ensures that data is not discarded in a systematic way that creates bias while also often increasing precision of the effect estimates due to increased power.

Limitations

This study has several limitations. First, the study is vulnerable to misclassification because it relies on self-reported patient information. Validated questionnaires, such as SLAQ for disease activity and BILD for disease damage, were used where possible. Additionally, information on covariates is collected only at the time of the survey, not at the time of becoming unemployed or disabled or at any time in between. As such, values of study covariates that can fluctuate over time (such as SLE disease activity or occupation) may not reflect the value at time of workforce exit. Non-reversible covariates (such as disease damage) may be overestimated as they continue accumulating. Additionally, the retrospective nature of some of the survey questions may leave open the possibility of recall bias. For example, survey respondents were asked to recall their occupations at the time of diagnosis.

Second, the cross-sectional design of the study limits the interpretations of the associations between specific organ damage and work loss. No causal relationships can be examined because the temporal relationship of organ damage and work loss cannot be definitively established.

A third limitation is the narrow scope of the BILD instrument, which measures disease damage. BILD contains information about major events – strokes, seizures, myocardial infarctions, end-stage renal disease requiring dialysis or renal transplant, etc. Thus, BILD has lower sensitivity for domains that also have less dramatic manifestations of damage, such as the neuropsychiatric domain. Subtle neuropsychiatric manifestations of SLE, such as cognitive dysfunction or memory impairment, cannot be assessed with BILD. However, there is some evidence that employment status in SLE is correlated with both of these more subtle manifestations that are not assessed (31, 34, 35).

Finally, while the patients were verified to have a diagnosis of SLE by examination of medical records, diagnoses of comorbidities were gathered by self-report without confirmation from external sources. Patients may report the presence of a symptom or comorbidity without any supporting clinical findings. Given that the GOAL study will continue to prospectively observe this cohort, it is possible that future iterations could incorporate some physician-observed measures.

CONCLUSION

This study has added to a growing body of literature on the impact of disease damage in the development of work loss among those with SLE. Because this community-based cohort is derived from a population-based registry, the results may be more generalizable to the larger population with lupus.

Cardiovascular damage, renal damage, and for those with low disease activity, neuropsychiatric damage were profoundly associated with work loss in this cohort, even after adjustment for confounders. Other types of organ damage (ocular, musculoskeletal, peripheral vascular, and gastrointestinal) were significantly associated with work loss in univariate analysis but not after adjustment for confounders.

Future research with longitudinal study designs may further elucidate the link between specific organ damage and work loss. Interventions to prevent specific types of organ damage known to influence work loss may have utility in increasing workforce participation in this population.

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Fig. Algorithm for Selection of Study Population

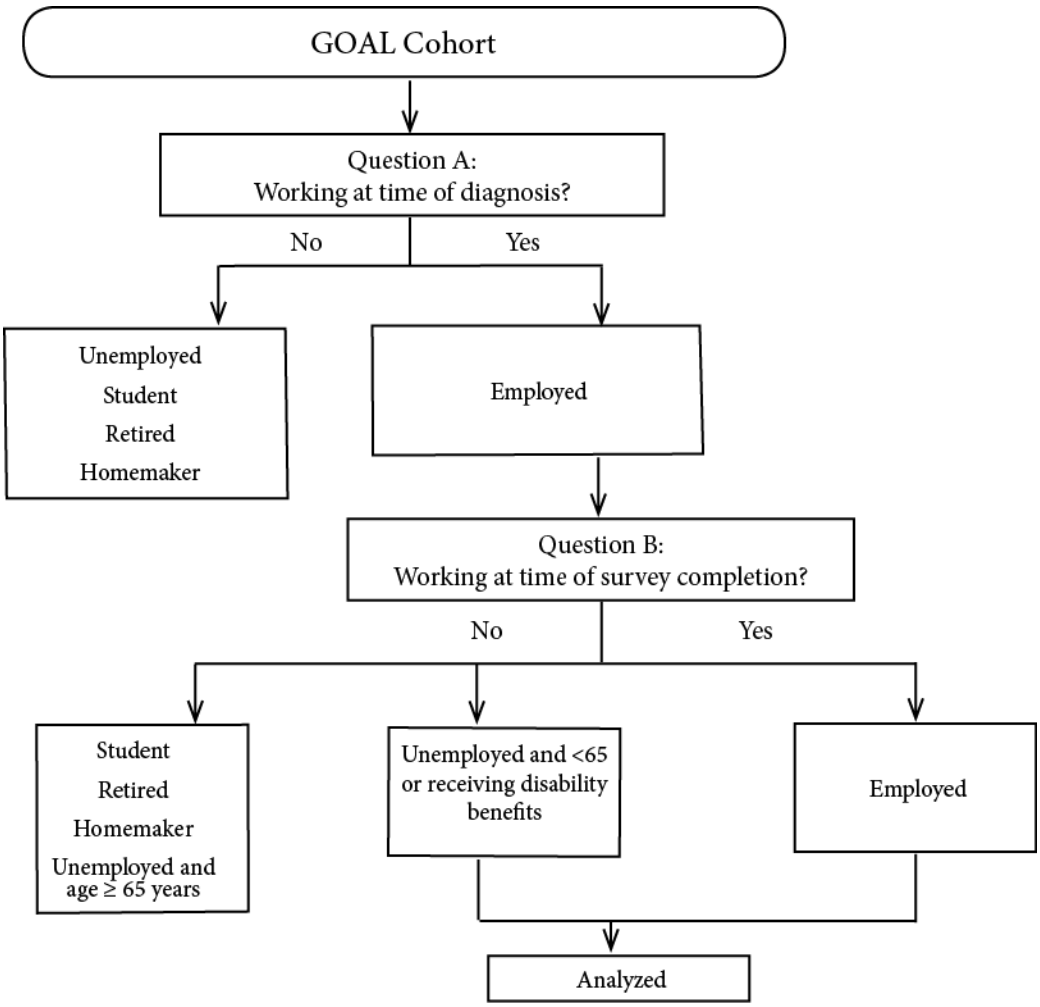

Table 1. Socio-Demographic and Clinical Characteristics by Employment Status

		Work Loss[a]	
	Overall	No	Yes
Characteristics	n = 463	n = 200	n = 263
Age at interview, years, mean (SD)	46.6 (10.0)	46.8 (9.6)	46.4 (10.3)
Age Categories at time of interview (%)			
18-34	72 (15.6)	25 (12.5)	47 (17.9)
35-49	204 (44.1)	104 (52.0)	100 (38.0)
50+	187 (40.4)	71 (35.5)	116 (44.1)
Female (%)	432 (93.3)	190 (95.0)	242 (92.0)
BMI, mean (SD)*	29.2 (7.5)	28.8 (7.4)	29.5 (7.6)
Race (%)			
African-American	368 (79.7)	145 (72.9)	223 (84.8)
White	66 (14.3)	45 (22.6)	21 (8.0)
Multi/Other	28 (6.1)	9 (4.5)	19 (7.2)
Education, years, mean (SD)	14.2 (2.8)	15.4 (3.2)	13.3 (2.2)
Marital status (%)			
Never Married	160 (34.6)	57 (28.5)	103 (39.2)
Married	154 (33.3)	84 (42.0)	70 (26.6)
Separated	27 (5.8)	6 (3.0)	21 (8.0)
Divorced	105 (22.7)	49 (24.5)	56 (21.3)
Widow	17 (3.7)	4 (2.0)	13 (4.9)
Occupational Physical Requirements (%)			
Sedentary	117 (27.7)	62 (34.6)	55 (22.5)
Low	231 (54.6)	91 (50.8)	140 (57.4)
Medium or greater	75 (17.7)	26 (14.5)	49 (20.1)
Age at SLE diagnosis, years, mean	33.2 (9.2)	33.7 (9.5)	32.8 (8.9)
Age at SLE diagnosis by categories, years (%)			
8-24	96 (21.1)	39 (19.9)	57 (22.0)
25-29	87 (19.1)	40 (20.4)	47 (18.1)
30-34	79 (17.4)	33 (16.8)	46 (17.8)
35-39	86 (18.9)	37 (18.9)	49 (18.9)
40+	107 (23.5)	47 (24.0)	60 (23.2)
Disease Duration, years, mean (SD)*	13.5 (8.6)	13.2 (8.5)	13.7 (8.6)
Disease Duration, year categories (%)			
0 - 8	143 (31.4)	59 (30.1)	84 (32.4)
8-12	83 (18.2)	43 (21.9)	40 (15.4)
12-16	77 (16.9)	31 (15.8)	46 (17.8)
16+	152 (33.4)	63 (32.1)	89 (34.4)
SLAQ Mean (SD)	17.9 (9.0)	14.6 (8.0)	20.3 (9.0)

		Work Loss[a]	
	Overall	No	Yes
Characteristics	n = 463	n = 200	n = 263
Self-reported smoking status (%)			
Never	319 (69.2)	149 (74.5)	170 (65.1)
Former	79 (17.1)	31 (15.6)	48 (18.3)
Current	62 (13.4)	19 (9.5)	43 (16.3)
Self-reported Comorbidities			
Emphysema	4 (0.9)	0 (0)	4 (1.5)
Asthma	59 (12.9)	24 (12.2)	35 (13.3)
Bronchitis	20 (4.4)	8 (4.1)	12 (4.6)
COPD	17 (3.7)	5 (2.6)	12 (4.6)
High Cholesterol	76 (16.6)	20 (10.2)	56 (21.3)
High Blood Pressure	266 (58.0)	94 (48.0)	172 (65.4)
Depression	175 (38.1)	40 (20.4)	135 (51.3)
Stomach Ulcers	23 (5.0)	5 (2.6)	18 (6.8)
"Liver Problems"	14 (3.1)	4 (2.0)	10 (3.8)
"Gall Bladder Problems"	18 (3.9)	3 (1.5)	15 (5.7)
Self-reported Organ System Damage			
BILD score, mean (median)	2.3 (2.5)	1.4 (1.7)	3.0 (2.7)
Presence of Organ Damage			
Ocular Damage	132 (28.6)	44 (22.1)	88 (33.5)
CNS Damage	78 (16.8)	19 (9.5)	59 (22.4)
Cardiovascular Damage	71 (15.3)	8 (4.0)	63 (2.04)
Pulmonary Damage	63 (13.6)	21 (10.5)	42 (16.0)
Musculoskeletal Damage	78 (17)	24 (12.2)	54 (20.7)
Skin Damage	42 (9.2)	15 (7.6)	27 (10.3)
Peripheral Vascular Damage	54 (11.7)	13 (6.5)	41 (15.6)
GI Damage	109 (23.6)	33 (16.6)	76 (28.9)
Renal Damage	37 (8.0)	5 (2.5)	32 (12.2)
Premature Gonadal Failure Damage	86 (35.2)	30 (31.9)	56 (37.3)
Malignancy Damage	33 (7.2)	14 (7.0)	19 (7.3)
Diabetes	49 (10.6)	14 (7.0)	35 (13.4)

		Work Loss[a]	
	Overall	No	Yes
Characteristics	n = 463	n = 200	n = 263
Current Medication use (%)			
Steroids	247 (55.4)	79 (41.4)	168 (65.9)
Plaquenil	306 (68.3)	135 (69.6)	171 (67.3)
Methotrexate	31 (7.3)	10 (5.3)	21 (8.9)
Cytoxan	8 (1.9)	1 (0.5)	7 (3.1)
Cyclosporine	1 (0.2)	0 (0)	1 (0.4)
Mycophenolate mofetil	56 (13.1)	25 (13.1)	31 (13.1)
Dapsone	8 (1.9)	2 (1.1)	6 (2.6)
Azathioprine	46 (10.8)	17 (9)	29 (12.2)
Belimumab	3 (0.7)	1 (0.5)	2 (0.9)
Rituximab	3 (0.7)	0 (0)	3 (1.3)
Anti-TNF	8 (1.9)	0 (0)	8 (3.4)
Osteoporosis medications	34 (7.8)	9 (4.7)	25 (10.2)
Vitamins	264 (59.1)	125 (64.1)	139 (55.2)
Vitamin D	264 (58.9)	116 (58.9)	148 (59.0)
Calcium	247 (54.6)	108 (55.1)	139 (54.3)

[a] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

Table 2. Crude Prevalence Odds Ratios for Work Loss[a] vs. No Work Loss in a Cohort of SLE Patients

	Unemployed/Work Disabled	
Characteristics	Prevalence Odds Ratio (95% CI)	p-value
Age at interview, per year	1.00 (0.98-1.01)	p = 0.64
Age Categories at time of interview		
18-34	1.96 (1.12-3.41)	p = 0.018
35-49	1.00 (Referent)	-
50+	1.70 (1.14-2.54)	p = 0.010
Female	0.61 (0.28-1.32)	p = 0.21
BMI, mean, per point	1.01 (0.99-1.04)	p= 0.30
Race		
African-American	1.00 (Referent)	-
White	0.30 (0.17-0.53)	p = <0.001
Multi/Other	1.37 (0.60-3.12)	p = 0.45
Education, per year attained	0.75 (0.69-0.81)	p = <0.001
Marital status		
Never Married	2.17 (1.38-3.41)	p = 0.001
Married	1.00 (Referent)	-
Separated	4.20 (1.61-10.98)	p = 0.003
Divorced	1.37 (0.83-2.26)	p = 0.21
Widow	3.90 (1.22-12.50)	p = 0.022
Occupational Physical Requirements		
Sedentary	1.00 (Referent)	-
Low	1.73 (1.11-2.72)	p = 0.016
Medium or greater	2.12 (1.17-3.86)	p = 0.014
Age at SLE diagnosis, per year	0.99 (0.97-1.01)	p = 0.28
Age at SLE diagnosis by age categories		
8-24	1.24 (0.69-2.24)	p = 0.47
25-29	1.00 (Referent)	-
30-34	1.19 (0.64-2.19)	p = 0.59
35-39	1.13 (0.62-2.05)	p = 0.70
40+	1.09 (0.62-1.92)	p = 0.78
Disease Duration, per year	1.01 (0.99-1.03)	p = 0.53
Disease Duration, year categories		
0 - 8	1.00 (Referent)	-
8-12	0.65 (0.38-1.13)	p = 0.13
12-16	1.04 (0.59-1.83)	p = 0.89
16+	0.99 (0.62-1.58)	p = 0.97
SLE activity (SLAQ) score, per point	1.08 (1.06-1.11)	p = <0.001

Characteristics	Unemployed/Work Disabled	
	Prevalence Odds Ratio (95% CI)	p-value
Self-reported smoking status		
Never	1.00 (Referent)	-
Former	1.34 (0.81-2.22)	p = 0.25
Current	1.96 (1.09-3.51)	p = 0.024
Self-reported Comorbidities		
Emphysema		
Asthma	1.10 (0.63-1.92)	p = 0.74
Bronchitis	1.12 (0.45-2.80)	p = 0.80
COPD	1.83 (0.63-5.27)	p = 0.27
High Cholesterol	2.38 (1.38-4.12)	p = 0.002
High Blood Pressure	2.05 (1.41-2.99)	p = <0.001
Depression	4.11 (2.69-6.28)	p = <0.001
Stomach Ulcers	2.81 (1.02-7.70)	p = 0.045
"Liver Problems"	1.90 (0.59-6.14)	p = 0.29
"Gall Bladder Problems"	3.89 (1.11-13.63)	p = 0.034
Self-reported Organ System Damage		
Organ damage (BILD) score, per point	1.45 (1.30-1.62)	p = <0.001
Presence of Damage by Organ System		
Ocular Damage	1.77 (1.16-2.70)	p = 0.008
CNS Damage	2.76 (1.58-4.80)	p = <0.001
Cardiovascular Damage	7.56 (3.53-16.20)	p = <0.001
Pulmonary Damage	1.62 (0.93-2.84)	p = 0.09
Musculoskeletal Damage	1.88 (1.12-3.17)	p = 0.018
Skin Damage	1.39 (0.72-2.70)	p = 0.32
Peripheral Vascular Damage	2.66 (1.38-5.11)	p = 0.003
GI Damage	2.04 (1.29-3.23)	p = 0.002
Renal Damage	5.4 (2.06-14.12)	p = 0.001
Premature Gonadal Failure Damage	1.27 (0.74-2.19)	p = 0.39
Malignancy Damage	1.03 (0.51-2.12)	p = 0.93
Diabetes	2.04 (1.06-3.90)	p = 0.032

Characteristics	Unemployed/Work Disabled	
	Prevalence Odds Ratio (95% CI)	p-value
Current Medication use[b]		
Steroids	2.74 (1.86-4.03)	p = <0.001
Plaquenil	0.90 (0.60-1.35)	p = 0.61
Methotrexate	1.74 (0.8-3.79)	p = 0.17
Cytoxan	5.83 (0.71-47.74)	p = 0.10
Mycophenolate mofetil	1.00 (0.57-1.77)	p = 0.99
Dapsone	2.47 (0.49-12.39)	p = 0.27
Azathioprine	1.41 (0.75-2.65)	p = 0.29
Belimumab	1.63 (0.15-18.09)	p = 0.69
Osteoporosis medications	2.32 (1.06-5.1)	p = 0.036
Vitamins	0.69 (0.47-1.01)	p = 0.06
Vitamin D	1.00 (0.69-1.47)	p = 0.99
Calcium	0.97 (0.67-1.41)	p = 0.87

[a] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

[b] some medications unable to be characterized because of paucity of use

Table 3. Adusted Prevalence Odds Ratios[a] for Work Loss[b] vs. No Work Loss in a Cohort of SLE Patients using Complete Case Analysis

	Adjusted Prevalence Odds Ratio (95% Confidence Interval)	p-value
Characteristics		
Education, per year attained	0.73 (0.65-0.81)	p = <0.001
Race		
African-American	1.00 (Referent)	-
White	0.40 (0.17-0.90)	p = 0.027
Multi/Other	1.56 (0.45-5.37)	p = 0.482
Self-reported Comorbidities		
High Blood Pressure	1.14 (0.67-1.93)	p = 0.64
Depression	4.71 (2.60-8.55)	p = <0.001
Current Medication use		
Steroids	2.06 (1.23-3.47)	p = 0.006
Presence of Damage by Organ System		
Ocular Damage	1.07 (0.58-1.95)	p = 0.84
Cardiovascular Damage	9.43 (3.46-25.71)	p = <0.001
Pulmonary Damage	0.82 (0.38-1.77)	p = 0.61
Musculoskeletal Damage	0.79 (0.37-1.69)	p = 0.55
Skin Damage	0.78 (0.31-1.95)	p = 0.59
Peripheral Vascular Damage	1.53 (0.60-3.89)	p = 0.37
GI Damage	1.46 (0.75-2.85)	p = 0.27
Renal Damage	6.29 (2.05-19.28)	p = 0.001
Diabetes	1.00 (0.43-2.33)	p = 1.00

[a] Each variable adjusted for the following: all other variables reported; self-reported CNS damage, self-reported lupus activity, and the interaction term of these two variables

[b] refers to those who were employed full or part time at diagnosis and who are currently

Table 4a. Adusted Prevalence Odds Ratios[a] for Work Loss[b] vs. No Work Loss in a Cohort of SLE Patients using Complete Case Analysis, Low Activity[c]

	Adjusted Prevalence Odds Ratio (95% Confidence Interval)	p-value
Characteristics		
Education, per year attained	0.77 (0.67-0.89)	p = <0.001
Race (%)		
African-American	1.00 (Referent)	-
White	0.10 (0.02-0.41)	p = 0.001
Multi/Other	0.81 (0.14-4.72)	p = 0.82
Self-reported Comorbidities		
High Blood Pressure	0.79 (0.36-1.73)	p = 0.55
Depression	4.22 (1.61-11.08)	p = 0.004
Current Medication use		
Steroids	2.12 (1.01-4.45)	p = 0.048
Self-reported Organ System Damage		
Presence of Damage		
Ocular Damage	0.90 (0.36-2.23)	p = 0.81
Neuropsychiatric Damage	8.74 (2.14-35.71)	p = 0.003
Cardiovascular Damage	29.26 (4.91-174.43)	p = <0.001
Pulmonary Damage	1.49 (0.41-5.36)	p = 0.54
Musculoskeletal Damage	0.81 (0.25-2.63)	p = 0.72
Skin Damage	1.00 (0.19-5.26)	p = 1.00
Peripheral Vascular Damage	0.96 (0.13-6.91)	p = 0.97
GI Damage	1.73 (0.65-4.62)	p = 0.27
Renal Damage	6.82 (1.86-25.00)	p = 0.004
Diabetes	0.63 (0.18-2.18)	p = 0.46

[a] Each variable adjusted for all other variables reported

[b] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

[c] refers to low disease activity, defined as less than the median SLAQ score of 17

Table 4b. Adusted Prevalence Odds Ratios[a] for Work Loss[b] vs. No Work Loss in a Cohort of SLE Patients using Complete Case Analysis, High Activity[c]

	Adjusted Prevalence Odds Ratio (95% Confidence Interval)	p-value
Characteristics		
Education, per year attained	0.71 (0.61-0.84)	p = <0.001
Race (%)		
African-American	1.00 (Referent)	-
White	0.91 (0.30-2.75)	p = 0.87
Multi/Other	2.78 (0.54-14.20)	p = 0.22
Education, years, mean (SD)	0.73 (0.61-0.86)	p = <0.001
Self-reported Comorbidities		
High Blood Pressure	1.64 (0.79-3.39)	p = 0.18
Depression	5.30 (2.52-11.15)	p = <0.001
Current Medication use		
Steroids	2.17 (1.05-4.46)	p = 0.036
Self-reported Organ System Damage		
Presence of Damage		
Ocular Damage	1.33 (0.60-2.94)	p = 0.49
Neuropsychiatric Damage	1.02 (0.42-2.48)	p = 0.96
Cardiovascular Damage	4.48 (1.40-14.33)	p = 0.011
Pulmonary Damage	0.65 (0.26-1.68)	p = 0.38
Musculoskeletal Damage	0.74 (0.28-1.93)	p = 0.53
Skin Damage	0.78 (0.27-2.30)	p = 0.66
Peripheral Vascular Damage	1.96 (0.70-5.44)	p = 0.20
GI Damage	1.33 (0.53-3.30)	p = 0.54
Renal Damage	4.12 (0.51-33.15)	p = 0.18
Diabetes	0.82 (0.26-2.60)	p = 0.74

[a] Each variable adjusted for all other variables reported

[b] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

[c] refers to high disease activity, defined as greater than the median SLAQ score of 17

Table 5. Adusted Prevalence Odds Ratios[a] for Work Loss[b] vs. No Work Loss in a Cohort of SLE Patients using Multiple Imputation

	Adjusted Prevalence Odds Ratio (95% Confidence Interval)	p-value
Characteristics		
Education, per year attained	0.74 (0.66-0.82)	p = <0.001
Race		
African-American	1.00 (Referent)	-
White	0.31 (0.14-0.67)	p = 0.003
Multi/Other	1.28 (0.41-4.03)	p = 0.67
Self-reported Comorbidities		
High Blood Pressure	1.22 (0.74-2.02)	p = 0.44
Depression	3.82 (2.17-6.72)	p = <0.001
Current Medication use		
Steroids	1.99 (1.20-3.29)	p = 0.008
Self-reported Organ System Damage		
Presence of Damage		
Ocular Damage	1.02 (0.58-1.82)	p = 0.94
Cardiovascular Damage	8.71 (3.41-22.21)	p = <0.001
Pulmonary Damage	0.74 (0.35-1.54)	p = 0.42
Musculoskeletal Damage	0.80 (0.39-1.63)	p = 0.54
Skin Damage	0.85 (0.35-2.06)	p = 0.72
Peripheral Vascular Damage	1.45 (0.62-3.40)	p = 0.39
GI Damage	1.64 (0.87-3.08)	p = 0.13
Renal Damage	6.29 (2.09-18.93)	p = 0.001
Diabetes	1.08 (0.48-2.46)	p = 0.85

[a] Each variable adjusted for the following: all other variables reported; self-reported CNS damage, self-reported lupus activity, and the interaction term of these two variables

[b] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

Table 6a. Adusted Prevalence Odds Ratios[a] for Work Loss[b] vs. No Work Loss in a Cohort of SLE Patients using Complete Case Analysis, Low Activity[c]

	Adjusted Prevalence Odds Ratio (95% Confidence Interval)	p-value
Characteristics		
Education, per year attained	0.76 (0.65-0.87)	p = <0.001
Race		
African-American	1.00 (Referent)	-
White	0.07 (0.02-0.26)	p = <0.001
Multi/Other	0.82 (0.14-4.95)	p = 0.83
Self-reported Comorbidities		
High Blood Pressure	0.71 (0.33-1.53)	p = 0.39
Depression	4.77 (1.83-12.43)	p = 0.001
Current Medication use		
Steroids	2.03 (0.96-4.31)	p = 0.07
Self-reported Organ System Damage		
Presence of Damage		
Ocular Damage	0.93 (0.38-2.26)	p = 0.87
Neuropsychiatric Damage	9.96 (2.72-36.49)	p = 0.001
Cardiovascular Damage	30.64 (5.42-173.11)	p = <0.001
Pulmonary Damage	1.24 (0.36-4.24)	p = 0.74
Musculoskeletal Damage	0.84 (0.27-2.62)	p = 0.76
Skin Damage	1.07 (0.20-5.74)	p = 0.94
Peripheral Vascular Damage	0.78 (0.14-4.41)	p = 0.78
GI Damage	1.56 (0.61-4.00)	p = 0.35
Renal Damage	8.03 (2.11-30.54)	p = 0.002
Diabetes	0.65 (0.19-2.24)	p = 0.49

[a] Each variable adjusted for all other variables reported

[b] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

[c] refers to low disease activity, defined as less than or equal to the median SLAQ score of 17

Table 6b. Adusted Prevalence Odds Ratios[a] for Work Loss[b] vs. No Work Loss in a Cohort of SLE Patients using Complete Case Analysis, High Activity[c]

	Adjusted Prevalence Odds Ratio (95% Confidence Interval)	p-value
Characteristics		
Education, per year attained	0.74 (0.63-0.86)	p = <0.001
Race		
African-American	1.00 (Referent)	-
White	0.74 (0.26-2.15)	p = 0.58
Multi/Other	1.68 (0.40-7.09)	p = 0.48
Self-reported Comorbidities		
High Blood Pressure	1.96 (0.98-3.90)	p = 0.06
Depression	3.98 (2.00-7.91)	p = <0.001
Current Medication use		
Steroids	2.07 (1.03-4.16)	p = 0.042
Self-reported Organ System Damage		
Presence of Damage		
Ocular Damage	1.18 (0.55-2.53)	p = 0.68
Neuropsychiatric Damage	1.17 (0.50-2.73)	p = 0.72
Cardiovascular Damage	4.27 (1.39-13.13)	p = 0.011
Pulmonary Damage	0.60 (0.24-1.47)	p = 0.26
Musculoskeletal Damage	0.79 (0.32-2.00)	p = 0.63
Skin Damage	0.86 (0.30-2.43)	p = 0.77
Peripheral Vascular Damage	1.75 (0.67-4.57)	p = 0.25
GI Damage	1.80 (0.75-4.32)	p = 0.19
Renal Damage	3.89 (0.53-28.66)	p = 0.18
Diabetes	0.91 (0.30-2.76)	p = 0.87

[a] Each variable adjusted for all other variables reported

[b] refers to those who were employed full or part time at diagnosis and who are currently unemployed or work disabled

[c] refers to high disease activity, defined as greater than the median SLAQ score of 17