Predictors of flare-related inpatient or emergency department stay in systemic lupus erythematosus: A real-world analysis of Medicaid claims in the United States

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Plain language summary

The results from this study identified groups of patients with systemic lupus erythematosus at higher risk of a flare-related inpatient (IP) stay/emergency department (ED) visit. Patients who had a prior ED visit or IP hospital stay in the prior year had the highest risk of a flare. Opioids and neurological disorders also increase the risk. There was a decreased risk among patients who were on a biologic medication. These results can be used to improve patient outcomes and reduce health care use and costs.

Implications for managed care pharmacy

This study identifies individual predictors (eg, opioid use and Black race) as well as combinations of risk factors (prior ED visits, IP stays, or other neurological disorders) that significantly increase the likelihood of having a flare-related IP/ED visit in the next year. This study also identifies the subgroups of patient with a particularly high probability for flare-related IP/ED visits and may provide the basis for more targeted disease management activities and input for clinical decision-making.

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ABSTRACT

BACKGROUND: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by multisystem inflammation. Medical management of SLE is based on reducing inflammation and tissue damage in the affected organs; however, medications used to treat SLE have been found to contribute to additional organ damage. Therefore, finding new ways to predict and prevent flares that require an inpatient (IP) stay or emergency department (ED) visit is critical for reducing the clinical and economic burden in patients with SLE.

OBJECTIVE: To identify risk factors of SLE flares requiring an IP/ED visit among a Medicaid-insured population with SLE.

METHODS: This retrospective study included patients from the Merative MarketScan Medicaid database (2013-2019). To capture patients at all stages of their SLE journey, all SLE claims for a patient were captured, and the index date was randomly selected among those claims that were at least 12 months after the first evidence of SLE. Patients were required to be continuously enrolled 1-year pre-index (year 1) and post-index (year 2). Demographics, clinical characteristics, and health care use and costs were measured in year 1, and flares requiring an IP/ED visit were identified in year 2 using the Garris algorithm. Multivariable logistic regression and classification and regression tree (CART) modeling were used to identify year 1 predictors and combination of factors, respectively, associated with flares-related IP/ED visits.

RESULTS: Of the 8,083 patients included in the study, 37.6% of patients (n = 3,039) had a flare. Logistic regression identified ED visits in year 1 as one of the strongest predictors of flares-related IP/ED visits in year 2 (odds ratio = 2.19 [95% CI = 1.93-2.49]). SLE treatment progression to biologics (0.54 [0.42-0.70]) was the strongest predictor of decreased odds. Other strong predictors included other neurological disorders (1.63 [1.43-1.87]), Black race (1.49 [1.32-1.68]), chronic kidney disease/renal failure (1.35 [1.10-1.66]), and opioid use (1.30 [1.17-1.45]). CART modeling identified patients with an ED visit, an IP admission, and a diagnosis of Elixhauser Comorbidity Index–defined other neurological disorders in year 1 as having the highest probability of a flare-related IP/ED visit in year 2 (probability = 0.708), whereas patients without an ED visit had the lowest probability (probability = 0.185).

CONCLUSIONS: Patients with the highest risk of a flare that required an IP/ED visit were

those with a prior ED visit, IP admission, and other neurological disorders. Modeling also identified patients with prior opioid use, Black patients, and patients without SLE medications as subgroups with a high risk of a flare requiring an IP/ED visit.

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with an estimated prevalence of 241 per 100,000 people in the United States.[1-3] SLE is characterized by multisystem inflammation affecting the skin, joints, kidneys, lungs, central nervous system, and hematopoietic system. It also has a relapsing–remitting course with cycles of lower disease status and periodic episodes of more active disease (ie, flares). Flares can increase in frequency and/or severity with disease progression.[4]

Medical management of SLE is based on reducing inflammation with the goal of preventing organ-damaging flares. The SLE treatment guidelines of the European Alliance of Associations for Rheumatology in 2019 recommend antimalarials for all patients with lupus. Glucocorticoids can provide rapid symptom relief, but the medium- to long-term aim should be minimized. Appropriate initiation of immunosuppressive drugs can expedite the tapering/discontinuation of glucocorticoids. Biologic agents should be considered for disease with inadequate control.[3] However, long-term use of some of these medications may contribute to organ damage that can increase the risk of a flare and reduce therapy adherence.[5]

Previous research has explored clinical and biomarker predictors of flares, with little consistency.[5,6] Although there have been some clinical factors and biomarkers that have demonstrated their use in clinical practice, they do not consistently identify the disease activity indicative of increasing flare risk in a generalizable population, and improving their predictive capabilities remains an area of ongoing research.[5,6] Furthermore, many promising clinical factors and biomarkers are not routinely collected and may impose an additional burden in the routine clinical workflow.

SLE flares that result in an inpatient (IP) admission or emergency department (ED) visit place a large clinical and economic burden on both patients and health care systems vs more mild flares that can be treated in the outpatient (OP) setting. Therefore, it is critical to focus flare prevention efforts on these more severe flares. The objective of this study was to identify predictors of those SLE flares requiring an IP/ED visit among a Medicaid-insured population with SLE using health plan administrative claims.

Methods

DATA SOURCE

This retrospective study used administrative claims data from the Merative MarketScan Multi-State Medicaid Database (Medicaid) from January 1, 2013, through December 31, 2019 (Supplementary Figure 1, available in online article). The Medicaid Database contains the pooled health care experience of more than 20 million Medicaid enrollees from multiple geographically dispersed states, including all IP admissions and services, OP services, and OP prescription drug claims. All patient records are deidentified, and a unique identifier links each patient's associated medical and pharmacy claims and enrollment information. Because this study used deidentified patient records, pursuant to the Health Insurance Portability and Accountability Act of 1996, institutional review board approval was not required. Study data were captured using *International Classification of Diseases, Ninth* and *Tenth Revisions, Clinical Modification* (ICD-9-CM/ICD-10-CM) codes, Current Procedural Terminology fourth edition codes, the Healthcare Common Procedure Coding System, and National Drug Code numbers.

STUDY DESIGN

This study identified a cohort of patients with prevalent SLE, specifically a population containing patients at any points in the SLE patient journey, rather than a population of patients with incident SLE. To this end, the index date was randomly selected among SLE service dates that were at least 12 months after the earliest identified SLE diagnosis. Patients were required to have at least 1 IP claim with an SLE diagnosis (ICD-9-CM: 710.0x or ICD-10-CM: M32-) or at least 2 nondiagnostic OP claims (ie, not diagnostic tests or screening) separated by 30-365 days. Patients were required to be at least age 18 years on index date and continuously enrolled for 12 months before the index date (year 1) and 12 months following the index date (year 2) (Supplementary Figure 1).[7] Because the cumulative oral corticosteroid (OCS) dose was considered a potential predictor of flares and an indicator of disease severity, patients were excluded if they had any OCS claims that were determined to be clinically invalid (eg, a prednisone-equivalent dose >200 mg/day or missing/zero value for the day's supply or quantity). There were no exclusion criteria for other SLE treatments because the dose was not a measured predictor of interest.

STUDY OUTCOMES

The primary study outcome was SLE flares that required an IP admission or ED visit in year 2. Flares that required

an IP/ED visit were chosen as the primary outcome because of the burden they place on both patients and health care systems. SLE flares and disease severity were identified using the Garris algorithm, a previously published real-world algorithm validated with administrative claims.[8] Flares were then further classified as those that required an IP admission with a primary diagnosis of SLE or a specified SLE-related condition (eg, end-stage renal disease or venous thrombosis) or an ED visit with a primary SLE diagnosis or secondary diagnosis for an SLE-related condition (see Supplementary Table 1 for SLE-related conditions).

Study Measures. Patient demographic characteristics were captured on index date and included age, sex, race, insurance plan type, and urbanicity. Comorbid conditions were identified by at least 1 claim with a diagnosis in any position during year 1. These included components of the Elixhauser Comorbidity Index (ECI) score, including cancer, chronic pulmonary disease, coagulopathy, congestive heart failure, deficiency anemia, depression, diabetes, drug abuse, fluid and electrolyte disorders, hypertension, hypothyroidism, liver disease, obesity, neurological disorders (including dementia, seizures, epilepsy, and neurological disorders affecting movement) and other neurological disorders, and peripheral vascular disorders.[9,10] Other measured comorbidities included SLE-related comorbidities as the components used in the SLE-specific risk-adjusted index developed by Ward[10]: anxiety, avascular necrosis, cardiovascular disease, chronic kidney disease, deep vein thrombosis/venous thromboembolic disease, fatigue, fever, fibromyalgia, fractures, glaucoma, headache, kidney transplant, lupus nephritis, osteoarthritis, osteoporosis, pleurisy/pleural effusion, pulmonary embolism, Raynaud disease, seizure, and thrombocytopenia.

SLE medication use in year 1 was measured in 2 ways. First medications were collected as a binary predictor indicating whether a patient had at least 1 claim for each class of medication (antimalarials, immunosuppressants, biologics, and systemic corticosteroids/OCSs). Second, SLE treatment progression was classified hierarchically by identifying the most advanced treatment a patient had received in year 1 (ie, no treatment, any antimalarial use but no immunosuppressant/biologic use, any immunosuppressant use but without biologic use, or any biologic use).[3] For example, if a patient had a claim for both an antimalarial medication and a biologic, they would be classified as having biologic use. Use of concomitant medications (antidepressants, antihypertensives, or opioids) were also reported in year 1. Additional measures of SLE disease activity in year 1 included cumulative OCS dosage and the total number of SLE flares in year 1, as defined by the Garris algorithm.[8]

All-cause and SLE-related health care resource use and costs were evaluated during year 1 as covariates. All-cause visits were defined as any IP or OP visit, regardless of diagnosis or treatment. SLE-related visits were defined as claims with an SLE diagnosis in any position, OP pharmacy claims for SLE treatments, or SLE-related comorbidities from the Ward SLE-specific risk-adjusted index[9,10] identified in any position of IP and ED claims. Costs included amounts paid by both health plans and patients for services, including medical and pharmacy costs. All costs were adjusted for inflation using the medical care component of the Consumer Price Index obtained from the US Bureau of Labor Statistics and standardized to 2019 US dollars.

STATISTICAL ANALYSIS

Demographic and baseline clinical characteristics were summarized descriptively. Counts and proportions were used to describe categorical variables, whereas means and SDs were used to describe continuous variables.

To identify factors associated with flares that required an IP/ED visit, 2 modeling approaches were implemented. First, multivariable logistic regression modeling was used to examine the linear relationship between year 1 predictors and the risk of a flare-related IP/ED visit in year 2; all covariates listed throughout the Methods section (demographic and clinical characteristics, SLE medications, SLE flares in year 1, health care resource utilization in year 1) were included in the logistic regression model (for a full list of covariates, see Supplementary Table 2). Second, a classification and regression tree (CART) model was used to generate a decision tree for predicting the risk of flares-related IP/ED visit based on the combination of predictors.[11] CART models select an optimal combination of predictors that can clearly identify subgroups of at-risk populations and, therefore, inform recommendations.[12] Additionally, CART models are not subject to the limitation of multicollinearity of a logistic regression model.

The study dataset was randomly split into training (75% of patients) and validation (remaining 25% of patients) datasets with which the CART model was fitted and validated. At each node, the tree was split on the predictor and split value that minimized the Gini impurity. The splitting process continued within each new data partition until the maximum tree depth was achieved. The tree was then pruned to avoid overfitting by penalizing the purity criterion using a complexity parameter, a factor of the total number of terminal nodes in the tree. The optimal complexity parameter was selected using 10-fold cross validation repeated 10 times. The tree's predictive performance was evaluated in the validation dataset using the area under the receiver

operator curve, also known and the C-statistic, and the Brier score.

The predicted probability of having a flare was computed for each patient in the validation dataset. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were computed at various predicted probability cutoffs for classification. Predicted probability at least 0.3 was used to classify patients as predicted to have an IP or ED flare. Lastly, the relative variable importance will be reported for all predictors included in the CART model, with the percent improvement reported for each variable as compared with the most important variable.

Descriptive analyses were conducted using WPS version 4.2 (World Programming), multivariable and CART analyses were conducted using R version 3.6.3, and the "rpart" package.

Results

DEMOGRAPHIC AND YEAR 1 CHARACTERISTICS

After applying patient selection criteria, the study identified 8,083 patients with SLE in the Medicaid database. Most patients were female (93.3%), and the mean (SD) age of patients was 40.9 (12.3) years (Table 1 and Supplementary Table 3). Overall, 46.9% of patients were Black, 38.3% were White, and 14.7% identified as another race. The most frequently observed year 1 comorbidities included hypertension (52.3%), anxiety (34.8%), depression (34.8%), deficiency anemia (26.1%), fibromyalgia (25.2%), and obesity (24.5%). SLE treatments commonly prescribed in year 1 included systemic corticosteroids (36.0%), antimalarials (55.2%), and immunosuppressants (32.3%); biologics were prescribed to 4.9% of patients. Of those without biologics, 28.8% were

TABLE 1 Select Demographics and Year 1 Characteristics (Full Table Available in the Supplementary Materials)

Characteristics and demographics	All patients (N = 8,083)	
Demographic characteristics[a]		
Age, mean SD, y	40.9	12.3
Female sex, n %	7,537	93.3
Race, n %		
White	3,097	38.3
Black	3,794	46.9
Other	1,192	14.7
Urbanicity, urban, n %	6,312	78.1
Clinical characteristics[b]		
Selected ECI conditions, n %		
Chronic pulmonary disease	1,937	24.0
Depression	2,809	34.8
Diabetes	1,375	17.0
Hypertension	4,225	52.3
Hypothyroidism	977	12.1
Obesity	1,982	24.5
Other neurological disorders[c]	1,387	17.2
Renal failure	840	10.4
SLE-related comorbidities, n %[d]		
Anxiety	2,816	34.8
Atherosclerosis	546	6.8
Cerebrovascular disease[e]	719	8.9
Endocarditis	774	9.6
Myocardial infarction	283	3.5
Pericarditis	206	2.5
Chronic kidney disease	1,093	13.5
Fibromyalgia	2,040	25.2
Fractures	455	5.6
Kidney transplant	50	0.6
Lupus nephritis	1,207	14.9
Osteoarthritis	1,916	23.7
Osteoporosis	440	5.4
Pleurisy/pleural effusion	396	4.9
Raynaud disease	495	6.1
Thrombocytopenia	500	6.2
Number of flares, mean SD	3.9	2.0

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TABLE 1 Select Demographics and Year 1 Characteristics (Full Table Available in the Supplementary Materials) *(continued)*

Characteristics and demographics	All patients (N = 8,083)	
Treatment characteristics[b]		
SLE treatments, n %		
Antimalarials	4,460	55.2
Biologics	397	4.9
Immunosuppressants	2,609	32.3
Systemic corticosteroids	2,907	36.0
Cumulative OCS dose[f] in 100 mg, mean SD	9.15	17.32
Most advanced SLE treatments, n %		
No antimalarial, immunosuppressant, or biologic use	2,905	35.9
Antimalarial (without immunosuppressant or biologic)	2,454	30.4
Immunosuppressant (without biologic use)	2,327	28.8
Biologic	397	4.9
Concomitant medications, n %		
Antidepressants	4,220	52.2
Antihypertensives	4,539	56.2
Opioids	4,148	51.3
All-cause health care utilization and costs[b]		
Patients with an IP admission, n %	2,128	26.3
Patients with an ED visit, n %	5,649	69.9
Total health care costs, mean SD, USD	$19,996	$59,337

[a]*Demographic characteristics were measured on the index date.*
[b]*Clinical characteristics, treatment characteristics, and health care utilization and costs were measured during the 12-month period before the index date.*
[c]*"Other" neurological conditions are defined in the ECI as neurological conditions other than dementia, seizures and epilepsy, or neurological disorders affecting movement.*
[d]*The SLE-related comorbidities were adapted from Ward 2000.*[10]
[e]*Cardiovascular disease is inclusive of cerebrovascular disease and myocardial infarction, as well as other cardiovascular-related conditions.*
[f]*OCS dosing was measured in prednisone-equivalent doses.*
ECI = Elixhauser Comorbidity Index; ED = emergency department; IP = inpatient; OCS = oral corticosteroid; SLE = systemic lupus erythematosus; USD = United States dollar; y = year.

TABLE 2 Frequency and Proportion of SLE Flare-Related IP/ED Visit in Year 2

Health care utilization	All patients (N = 8,083)	
Patients with an SLE flare-related IP/ED visit, n %	3,039	37.6
Patients with a flare-related IP admission, n %	738	9.1
Patients with a flare-related ED visit, n %	2,748	34.0

ED = emergency department; IP = inpatient; SLE = systemic lupus erythematosus.

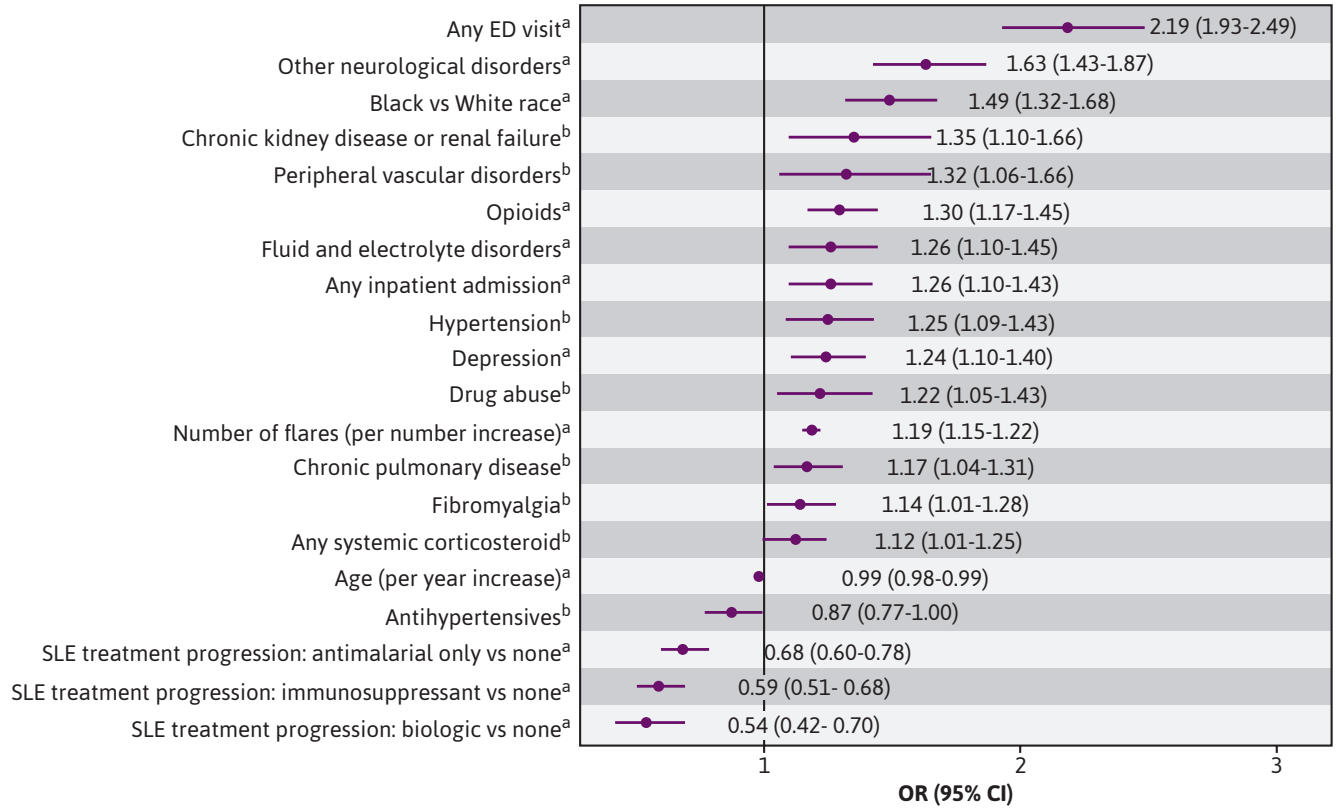
prescribed immunosuppressants; and, of the remainder, 30.4% were prescribed only antimalarials. Notably, 51.3% of patients were prescribed an opioid in year 1.

In year 1, 26.3% of patients had at least 1 all-cause IP admission, and 69.9% had at least 1 all-cause ED visit.[13] Average total all-cause health care costs during year 1 were $19,996 (SD = $59,337) (Table 1 and Supplementary Table 3).

PREDICTORS OF SLE FLARE-RELATED IP/ED VISITS: LOGISTIC REGRESSION MODEL

In year 2, 37.6% of patients (n = 3,039) had an SLE flare that required an IP/ED visit, with 9.1% of patients specifically having at least 1 flare-related IP stay and 34.0% having at least 1 flare-related ED visit (Table 2). Results from adjusted logistic regression models indicate that patients with at least 1 ED visit in year 1 had more than twice the odds of having a flare-related IP/ED visit in year 2 (odds ratio [OR] = 2.19, 95% CI = 1.93-2.49) than those without a year 1 ED visit. Compared with no SLE treatment, SLE treatment with biologics (OR = 0.54, 95% CI = 0.42-0.70), immunosuppressants (OR = 0.59, 95% CI = 0.51-0.68), or antimalarials (OR = 0.54, 95% CI = 0.42-0.70) was associated with decreased odds of a flare-related IP/ED visit in year 2. The other predictors of a flare-related IP/ED visit in year 2 were ECI-defined other neurological disorders (OR = 1.63, 95% CI = 1.43-1.87), Black race (OR = 1.49, 95% CI = 1.32-1.68), and chronic kidney disease/renal failure (OR = 1.35, 95% CI = 1.10-1.66). Of note, total health care costs (per 10% increase) in year 1 were not associated with the odds of a flare-related IP/ED visit in year 2. Full results from the adjusted logistic regression models are reported in Figure 1 (significant factors; $P < 0.05$) and Supplementary Table 2 (full model results).

FIGURE 1 Associations Between Year 1 Patient Characteristics With Any SLE Flare-Related IP/ED Visit in Year 2 Based on Logistic Regression Modeling



Logistic regression modeling was used to identify significant predictors of IP or ED flares, and the ORs and 95% CIs are reported for the statistically significant variables (P<0.05). Full model results can be found in Supplementary Table 2.

[a]P < 0.001.

[b]P < 0.05.

CI = confidence interval; ED = emergency department; IP = inpatient; OR = odds ratio; SLE = systemic lupus erythematosus.

PREDICTORS OF SLE FLARE-RELATED IP/ED VISITS: CART MODEL

The variable importance of year 1 characteristics was assessed and reported in Table 3. Variable importance identified opioids (variable importance = 1.00), other neurological disorders (0.96), any ED visit (0.92), any IP admission (0.89), and depression (0.64) as the variables given the strongest weight in CART modeling (Table 3).

The CART model identified combinations of attributes useful to determining the risk of year 2 IP or ED SLE flares. Patients with a year 1 ED visit, a year 1 IP admission, and evidence of other neurological disorders had the highest probability of a flare requiring an IP/ED visit in year 2 (probability = 0.708), whereas patients without a year 1 ED visit had the lowest probability of a year 2 flare-related IP/ED visit (probability = 0.185) (Figure 2). The C-statistic for selected covariates was 0.72.

Discussion

The results of this analysis highlight the substantial unmet need for improved management of SLE among Medicaid patients, as demonstrated by the fact that more than one-third of the SLE patients in our study had at least 1 SLE flare-related IP/ED visit during year 2. ED visits during year 1 were found to be an important predictor of year 2 IP or ED SLE flares in both the logistic regression and CART models.

TABLE 3 Variable Importance of Year 1 Covariates Potentially Related to Any Flare-Related Inpatient or ED Visits in Year 2 Based on Classification and Regression Tree Model

Predictor	Variable importance
Opioids	1.000
Other neurological disorders[a]	0.964
Any ED visit	0.918
Any inpatient admission	0.892
Depression	0.643
Chronic kidney disease or renal failure	0.318
Any systemic corticosteroid	0.135
Lupus nephritis	0.099
Race	0.090
Hypertension	0.089
Pericarditis	0.027

The following characteristics were also included in the model but had a variable importance of 0.000: aged at least 45 years, aged at least 65 years, sex, insurance plan type, cancer, chronic pulmonary disease, coagulopathy, congestive heart failure, diabetes, drug abuse, liver disease, peripheral vascular disorders, anxiety, atherosclerosis, cerebrovascular disease/stroke/transient ischemic attack, endocarditis, myocardial infarction, fibromyalgia, fractures, kidney transplant, osteoarthritis, osteoporosis, pleurisy/pleural effusion, Raynaud disease, thrombocytopenia, antidepressants, and antihypertensives.

[a]*"Other" neurological disorders are defined in the Elixhauser Comorbidity Index as neurological conditions other than dementia, seizures and epilepsy, or neurological disorders affecting movement.*

ED = emergency department.

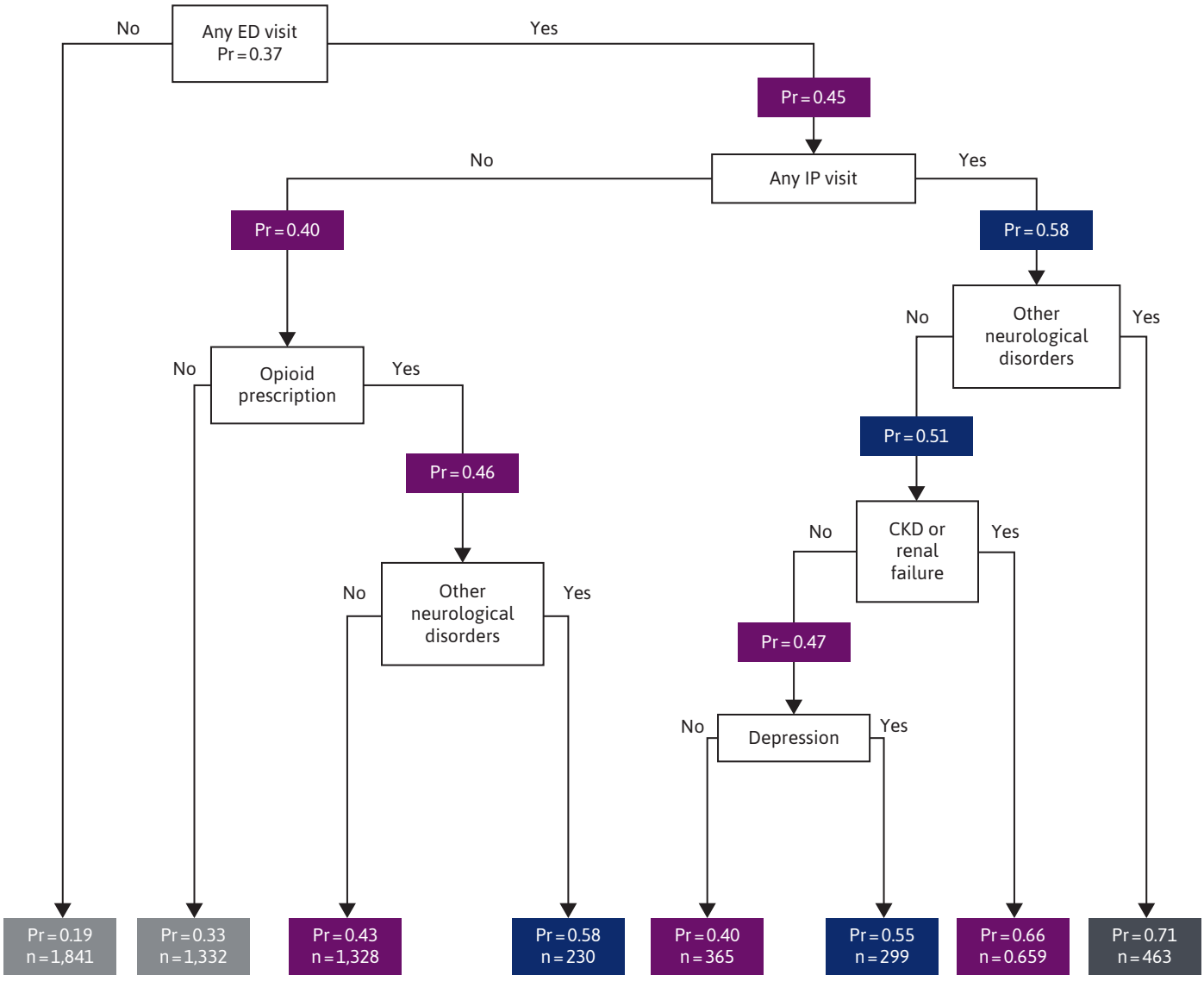
Our results provide data on opioids and acute care use among patients with SLE. In this study, opioid use was identified as the factor with the highest variable importance but was only included in the classification tree for those patients with an ED visit and no IP admission. This supports previous research reporting that pain management is one of the major reasons for ED use among patients with SLE.[14] Additionally, more than half of the patients with SLE had evidence of opioid use during year 1. Although it is unclear whether the opioids were prescribed for the treatment of SLE, the high proportion of patients with SLE with evidence of opioid use during year 1 may be indicative of patients with SLE attempting to manage significant pain. Previous work has shown a similarly high use of opioids among patients with SLE, despite opioids not being indicated for the treatment of long-term musculoskeletal pain.[15,16] This provides actionable insight by identifying patients with prior opioid use as potential targets for intervention to decrease flare-related IP/ED visits.

Another interesting finding from this study was that mental health, specifically depression (OR = 1.24, 95% CI = 1.10-1.40), was a more important predictor in the logistic regression model than several physical conditions, such as cancer, congestive heart failure, diabetes, obesity, cerebrovascular disease/stroke/transient ischemic attack, kidney transplant, lupus nephritis, and osteoarthritis. Depression was also selected for inclusion by the CART models. Those patients who had an ED visit, an IP visit, another neurological disorder, chronic kidney disease or renal failure, and depression had a 55% probability of having a flare-related IP/ED visit, compared with a 40% probability among those without depression. This highlights the importance of comprehensively managing mental health for patients with SLE.

Among the demographic characteristics of Medicaid-insured patients with SLE, Black race was found to be a significant predictor of IP or ED flares in the logistic regression model. This increased risk of SLE flare-related IP/ED visits among Black patients is consistent with prior literature showing that Black patients are not only more likely to develop SLE flares but also to have a higher risk of more severe disease, including irreversible organ damage, end-stage renal disease, and death.[17-22] Improving disease management among Black patients, including reducing SLE flares, is critical to reducing the overall and disproportionate disease burden. However, despite the increased risk observed in the logistic regression model, Black race did not have high variable importance in the CART model (variable importance = 0.090) and was not included in the predictive tree. Previous research has shown that non-White patients with SLE have less access to primary care,[23] which, combined with the variable importance, may suggest that race is acting as a proxy for more critical health care use (eg, ED visits and IP admissions) and is an area on which future research could be focused. Therefore, SLE outcomes for Black patients with SLE could be improved through greater access to primary care as well as providers identifying those patients most at risk based on the CART model rather than relying broadly on race as a risk factor for IP or ED flares.

This study also highlights the potential to reduce flare-related IP/ED visits through improved pharmacological treatment. In the logistic regression model, more advanced pharmacological treatment in year 1 was associated with a decreased risk of a flare-related IP/ED visit in year 2. Biologic treatment compared with no treatment reduced flare risk by 46% compared with 41% for immunosuppressants and 32% for antimalarials. This suggests a positive association of IP or ED flare reduction with the use of advanced pharmacologic treatment for SLE. With the information gained from this study, future research should focus on medication adherence and discontinuation in relation to the timing of the SLE flare.[24,25]

FIGURE 2 Classification and Regression Tree Model of Associations Between Year 1 Patient Characteristics and Any SLE Flare-Related IP/ED Visit in Year 2



Classification and regression tree model with complexity factor selected using 10-fold cross validation repeated 10 times. The minimum terminal node size is 50. The sample size is N = 8,083 (n = 3,039 with a year 2 IP or ED SLE flare; n = 5,044 without).

"Other" neurological disorders are defined in the Elixhauser Comorbidity Index as neurological conditions other than dementia, seizures and epilepsy, or neurological disorders affecting movement.

CKD = chronic kidney disease; ED = emergency department; IP = inpatient; Pr = probability; SLE = systemic lupus erythematosus.

LIMITATIONS

There are several limitations associated with the results of this study. Clinical characteristics and identification of SLE flares were ascertained based on diagnosis codes, procedure codes, and pharmacy prescriptions in claims, which are subject to data coding limitations and data entry error; this may have resulted in an underestimation of flares because of a lack of information on biomarkers previously used to identify SLE flares. Similarly, as treatment outcomes are based on claims, we assume that patients took medications

as prescribed; there was no confirmation through chart review or patient contact confirming that patients took the medications. Second, results from this study are limited to patients with SLE receiving Medicaid coverage in select states and, therefore, are not representative of all patients with Medicaid or SLE. Results may not be generalizable to patients with SLE with other insurance types or without health insurance coverage. Additionally, because patients were required to have 2 years of continuous enrollment, there may be survivorship bias because patients who had more severe disease and died during the study period were not eligible for inclusion. Finally, the logistic regression and CART models were limited to predictors that are reported in administrative claims, which does not include social determinants of health, such as income and access to care, as well as other predictors of flares (eg, laboratory values).

Conclusions

This study examined a broad array of patient-level demographic, clinical, and pharmacological risk factors, and identified the most important predictors of flare-related IP/ED visits using 2 predictive methodologies. From the CART model, patients with a prior ED visit, IP admission, and a diagnosis for an ECI-defined other neurological disorder had the highest probability (70.8%) of a flare-related IP/ED visit and represent a population that would benefit from targeted intervention. Additionally, in logistic regression models, patients with SLE with prior opioid use and Black patients with SLE were identified as specific subgroups with a high risk of a flare-related IP/ED visit, indicating that these groups need improved disease management. Finally, more advanced pharmacological SLE treatments, particularly biologic therapy, was associated with a lower likelihood of a flare-related IP/ED visit, highlighting a treatment effect for effective management of SLE and flare reduction.

DISCLOSURES

This study was funded by AstraZeneca.

Dr Wu and Dr Bryant are current employees of AstraZeneca and may own stock, options, or both. At the time of the study, Ms Perry and Ms Zimmerman were employed by IBM Watson Health, which received funding from AstraZeneca to conduct this study.

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