Reasons for Hospitalization and In-Hospital Mortality in Adult Systemic Lupus Erythematosus

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**Objective.** Systemic lupus erythematosus (SLE) is an autoimmune disease with an increased risk of hospitalization. Multiple studies have reported SLE flare, infection, and cardiovascular (CV) events as the most common reasons for hospitalization. The aim of this study was to use a large US population–based database to comprehensively analyze all indications for adult SLE hospitalization and reasons for in-hospital mortality.

**Methods.** We conducted a retrospective study of SLE hospitalizations in 2017 from the National Inpatient Sample database. The "reason for hospitalization" and "reason for in-hospital mortality" in patients with SLE were divided into 19 categories based on their principal International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) diagnosis.

**Results.** A total of 180975 hospitalizations carried either a principal or secondary ICD-10 code for SLE. The leading reasons for hospitalization were CV (16%), rheumatologic (13%), infectious (11%), respiratory (10%), and gastrointestinal (10%). SLE itself was the principal diagnosis in only 6% of the hospitalizations. In-hospital death occurred in 1 of every 50 SLE hospitalizations. Infectious (37%) and CV diagnoses (21%) were the most common reasons for in-hospital death, with sepsis being the most frequent reason for death.

**Conclusion.** This analysis represents the only report to date that comprehensively categorizes the reasons for hospitalization and reasons for in-hospital mortality of patients with SLE on a US national level. SLE itself was the principal diagnosis for only a small percentage of hospitalizations. CV diagnoses were the most common reason for hospitalization. In-hospital death occurred in 1 of every 50 SLE hospitalizations. Infectious and CV diagnoses were the most common reason for in-hospital death.

# INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease that poses an increased risk of hospitalization (1). Multiple studies have reported SLE flare, infection, and cardiovascular (CV) events as the most frequent reasons for hospitalization (2-13). Unfortunately, many studies of SLE are limited because they are derived exclusively from tertiary referral hospitals or from small sample sizes (1,6,8,9,14). Additionally, studies that have examined SLE on a national level fail to analyze all reasons for hospitalization (2-4,7,10,11,15). The aim of this study was to use a large US population–based database to comprehensively analyze all indications for adult SLE hospitalization and reasons for in-hospital mortality.

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### MATERIALS AND METHODS

**Data source.** We conducted a retrospective study of adult SLE hospitalizations in 2017 in acute care hospitals across the United States from the National Inpatient Sample (NIS) database. An overview of the NIS database is available online at https:// www.hcup-us.ahrq.gov. The NIS was created and is maintained by the Agency for Healthcare Research and Quality and is the largest publicly available all-payer inpatient database in the United States. It was designed as a stratified probability sample to be representative of all nonfederal acute care hospitals nationwide. Hospitals are stratified according to ownership/ control, bed size, teaching status, urban/rural location, and geographic region. A 20% probability sample of all hospitals within

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# SIGNIFICANCE & INNOVATIONS

- This analysis represents the only report to date that comprehensively categorizes the reasons for hospitalization and reasons for in-hospital mortality of patients with SLE on a US national level.
- SLE itself was the principal diagnosis in only 6% of the hospitalizations. The overwhelming majority of both hospitalizations and deaths involving patients with SLE were for nonrheumatologic reasons.
- We found leading reasons for hospitalization were CV (16%), rheumatologic (13%), infectious (11%), respiratory (10%), and gastrointestinal (10%).
- In-hospital death occurred in 1 of every 50 SLE hospitalizations.
- Infectious diagnoses (37%) and CV diagnoses (21%) were the most common reasons for in-hospital death. Specifically, sepsis was the most frequent reason for death.

each stratum is then collected. All discharges from these hospitals were recorded and then weighted to ensure that they were nationally representative. The 2017 NIS sampling frame includes data from 47 statewide data organizations (46 states plus the District of Columbia), which covers more than 97% of the US population. One principal diagnosis and up to 39 secondary diagnoses were recorded for each hospitalization using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10). The principal diagnosis was the main discharge ICD-10 code for the hospitalization. Secondary diagnoses were the ICD-10 codes for any diagnoses other than the principal diagnosis. There is no reliable mechanism to distinguish secondary diagnoses that antedated the hospital admission from those that had onset during the index admission. Because all patient data in NIS are deidentified and publicly available, institutional review board approval was not sought.

Inclusion criteria and study variables. All hospitalizations in 2017 with a principal or secondary diagnosis of SLE were included. We used the following ICD-10 codes to identify SLE: M32, M32.1, M32.10, M32.11, M32.12, M32.13, M32.14, M32.15, M32.19, M32.8, and M32.9. Exclusion criteria was age of less than 18 years, as we were focusing on adult lupus. Descriptive statistics collected include age, gender, race, length of stay (LOS), total charges, in-hospital mortality, and ICD-10 codes. The "reason for hospitalization" and "reason for in-hospital mortality" in patients with SLE were divided into 19 categories based on their principal ICD-10 diagnosis. ICD-10 codes are composed of seven digits: the first three digits indicate the disease/organ category and always start with a letter. The fourth to sixth digits add details, and the seventh digit is laterality or episode of care. ICD-10 codes were grouped into organ system/disease categories by the first three digits as follows:

- Infectious = A00-B99: Certain infectious and parasitic diseases
- Hematology/Oncology = C00-D49: Neoplasms/D50-D89: Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
- Endocrine = E00-E89: Endocrine, nutritional, and metabolic diseases
- Psychiatry = F01-F99: Mental, behavioral and neurodevelopmental disorders
- Neurologic = G00-G99: Diseases of the nervous system
- Eye/Ear = H00-H59: Diseases of the eye and adnexa/ H60-H95: Diseases of the ear and mastoid
- CV = I00-I99: Diseases of the circulatory system
- Respiratory = J00-J99: Diseases of the respiratory system
- Gastrointestinal = K00-K95: Diseases of the digestive system
- Skin = L00-L99: Diseases of the skin and subcutaneous tissue
- Rheumatologic = M00-M99: Diseases of the musculoskeletal system and connective tissue; the SLE ICD-10 codes M32.1-M32.9 are a subset of the larger rheumatologic category
- Genitourinary (GU) = N00-N99: Diseases of the genitourinary system
- Obstetrics (OB) = O00-O9A: Pregnancy, childbirth, and the puerperium
- Perinatal = P00-P96: Certain conditions originating in the perinatal period
- Congenital = Q00-Q99: Congenital malformations, deformations, and chromosomal abnormalities
- Other = R00-R99: Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified
- Injury & poisoning = S00-T88: Injury, poisoning, and certain other consequences of external causes

Hospitalization	SLE Hospitalizations
Characteristics	(n = 180 975)
Women, n (%)	160 155 (88%)
Age, mean in years	52
Age distribution, n (%)	
- Age 18-40 y	47 205 (26%)
Age 40-60 y	67 300 (37%)
Age 60-80 y	56 500 (31%)
Age >80 v	9970 (6%)
Race (%)	
White	87 335 (48%)
African American	54 685 (31%)
Hispanic	23 460 (13%)
Asian or Pacific Islander	4470 (2.5%)
Native American	1210 (0.6%)
Other	5180 (3%)
	( )
Length of stay, mean days	5.4
Total charges, mean dollars	\$61 309

**Table 1.** Weighted descriptive characteristics of SLE hospitali-zations in 2017

Abbreviation: SLE, systemic lupus erythematosus.

- Accidents = V00-Y99: External causes of morbidity
- Health services = Z00-Z99: Factors influencing health status and contact with health services

**Outcomes.** Five outcomes were studied: (a) quantification of the prevalence of SLE hospitalizations and in-hospital mortality, (b) description of demographic characteristics of hospitalized patients with SLE, (c) identification of the most frequent principal ICD-10 diagnoses, (d) comprehensive analysis of the "reasons for hospitalization" and the "reasons for in-hospital mortality" by principal diagnosis category, and (e) quantification of the economic burden of SLE hospitalizations.

**Statistical analyses.** Analyses were performed using Stata, version 16 (StataCorp). Age is not normally distributed in the NIS, so we reported age in both mean and quartiles. NIS is based on a complex sampling design that includes stratification, clustering, and weighting. This software facilitates analysis to produce nationally representative results, means, ranges, and percentages.

#### RESULTS

After weighting, there were 35 million discharges documented in the 2017 NIS database. Of those, 180975 (0.5%) hospitalizations carried either a principal or secondary ICD-10 code for SLE. Patients were female 88% of the time, with a mean age of 52 years (Table 1). The racial breakdown of patients with SLE was as follows: White 48%, African American 31%, Hispanic 13%, Asian or Pacific Islander 2.5%, Native American 0.6%, and other 3%. Racial data were missing for 2.5% of the patients. The mean LOS was 5.4 days. The mean total hospital charges were \$61309. The top five principal ICD-10 diagnoses (Table 2) were sepsis unspecified organism A41.9 (n = 12000), SLE unspecified M32.9

Table 2.	Top principal ICD-10 diagnoses in SLE hospitalizations

Top Principal ICD-10 Diagnoses in SLE Hospitalizations	Weighted Number of Hospitalizations
Sepsis, unspecified organism A41.9	12 000
SLE, unspecified M32.9	4345
Pneumonia J18.9	3705
Acute kidney failure unspecified N17.9	3695
Glomerular disease in SLE M31.24	3215
Chronic obstructive pulmonary disease with (acute) exacerbation J44.1	2610
Hypertensive heart and chronic kidney disease with heart failure and stage 1 through 4 chronic kidney disease, or unspecified chronic kidney disease 113.0	2560
Non-ST elevation myocardial infarction I21.4	2200
Hypertensive heart disease with heart failure I11.0	2070
Urinary tract infection, site not specified N39.0	2010

Abbreviations: ICD-10, International Classification of Diseases, Tenth Revision, Clinical Modification; SLE, systemic lupus erythematosus.

nosis category (n = $180975$ )		
ICD-10 Diagnosis Category	Weighted Number (%) of Hospitalizations in SLE	
Cardiovascular	29 220 (16%)	
Rheumatologic	22 830 (13%)	
Infection	19 715 (11%)	
Gastrointestinal	18 195 (10%)	
Respiratory	17 430 (10%)	
Injury/poison	15 475 (9%)	
Genitourinary	10 330 (6%)	
Hematology/oncology	8070 (4%)	
Other	7860 (4%)	
Endocrine	7520 (4%)	
Neurologic	6150 (3%)	
Obstetrics	6115 (3%)	
Psychiatry	5425 (3%)	
Skin	4875 (3%)	
Health services	1225 (1%)	
Eye/ear	390 (0.2%)	
Congenital	150 (0.08%)	
Perinatal	0 (0%)	

**Table 3.** Reason for hospitalization of patients with SLE by diagnosis category (n = 180975)

Abbreviations: ICD-10, International Classification of Diseases, Tenth Revision, Clinical Modification; SLE, systemic lupus erythematosus.

Accident

0 (0%)

(n = 4345), pneumonia unspecified organism J18.9 (n = 3705), acute kidney failure N17.9 (n = 3695), and lupus nephritis M31.24 (n = 3215).

**Reasons for hospitalization by principal diagnosis category.** The reasons for hospitalization of patients with SLE were separated into 19 broad categories based on their principal diagnosis as follows (Table 3): CV, 29 220 (16%) rheumatologic, 22 830 (13%); infectious, 19715 (11%); gastrointestinal, 18 195 (10%); respiratory, 17 430 (10%); injury and poisoning, 15 475 (9%); GU, 10 330 (6%); hematology/ oncology, 8070 (4%); other, 7860 (4%); endocrine, 7520 (4%); neurologic, 6150 (3%); OB, 6115 (3%); psychiatric, 5425 (3%); skin, 4875 (3%); health services, 1125 (1%); eye and ear, 390 (0.2%); congenital, 150 (0.08%); perinatal, 0 (0%); and accidents, 0 (0 %).

**Mortality.** A total of 3630 (2%) patients with a principal or secondary ICD-10 code for SLE experienced in-hospital mortality. Those patients were female 86% of the time and had a mean age of 61 years. Their mean LOS was 8.3 days. The mean total hospital charges of deceased patients with SLE were \$143086. The top five principal ICD-10 diagnoses (Table 4) in patients with SLE experiencing in-hospital mortality were sepsis A41.9 (n = 935); acute respiratory failure with hypoxia J96.01 (n = 110); acute and chronic respiratory failure with hypoxia J96.21 (n = 100); hypertensive heart and chronic kidney disease with heart failure and stage 1 through 4 chronic kidney disease, or unspecified chronic kidney disease I13.0 (n = 70); and cardiac arrest, cause unspecified I46.9 (n = 65).

Table 4.	Top principal ICD-10	diagnoses in patients with SI	_E with in-hospital mortality
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Top Principal ICD-10 Diagnoses in SLE With In-Hospital Mortality	Weighted Number of Hospitalizations
Sepsis, unspecified organism A41.9	935
Acute respiratory failure with hypoxia J96.01	110
Acute and chronic respiratory failure with hypoxia J96.21	100
Hypertensive heart and chronic kidney disease with heart failure and stage 1 through 4 chronic kidney disease, or unspecified chronic kidney disease I13.0	70
Cardiac arrest, cause unspecified 146.9	65
Non-ST elevation myocardial infarction I21.4	65
Acute kidney failure unspecified N17.9	60
Sepsis due to Pseudomonas A41.52	55
Sepsis due to Methicillin susceptible Staphylococcus aureus A41.01	50
Gram-negative sepsis, unspecified A41.50	50

Abbreviations: ICD-10, International Classification of Diseases, Tenth Revision, Clinical Modification; SLE, systemic lupus erythematosus.

**Reasons for in-hospital mortality by principal diagnosis category.** The reasons for in-hospital mortality for the cohort of 3630 deceased patients with SLE were separated into 19 broad categories based on their principal diagnosis as follows (Table 5): infectious, 1325 (37%); CV, 755 (21%); respiratory, 470 (13%); gastrointestinal, 260 (7%); injury and poisoning, 260 (7%); hematology/oncology, 190 (5%); rheumatologic, 130 (4%); GU, 85 (2%); neurologic, 70 (2%); endocrine, 40 (1%); other, 30 (0.8%); eye and ear, 5 (0.1%); skin, 5 (0.1%); OB, 5 (0.1%); psychiatric, 0 (0%); perinatal, 0 (0%); congenital, 0 (0%); accidents, 0 (0%); and health services, 0 (0%).

**CV category and SLE.** The CV category (ICD-10 codes I00-I99) was the leading reason for hospitalization of patients with SLE, accounting for 16% of admissions and 21% of in-hospital mortality. Non–ST segment myocardial infarction (MI) I21.4 and hypertensive heart failure I13.0 were frequent diagnoses for both hospitalizations and mortality.

Table 5.	Reason for SLE in-hospital mortality by principal diagnosis
category	(n = 3630)

ICD-10 Principal Diagnosis	Weighted Number (%)
Category	SLE In-Hospital Mortality
Infections	1325 (37%)
Cardiovascular	755 (21%)
Respiratory	470 (13%)
Gastrointestinal	260 (7%)
Injury/poison	260 (7%)
Hematology/oncology	190 (5%)
Rheumatologic	130 (4%)
Genitourinary	85 (2%)
Neurologic	70 (2%)
Endocrine	40 (1%)
Other	30 (0.8%)
Eye/ear	5 (0.1%)
Skin	5 (0.1%)
Obstetrics	5 (0.1%)
Psychiatry	0 (0%)
Perinatal	0 (0%)
Congenital	0 (0%)
Accidents	0 (0%)
Health services	0 (0%)

Abbreviations: ICD-10, International Classification of Diseases, Tenth Revision, Clinical Modification; SLE, systemic lupus erythematosus. **Rheumatologic category and SLE.** The rheumatologic category (ICD-10 codes M00-M99) was the second most common reason for hospitalization of patients with SLE, accounting for 13% of hospitalizations and 4% of mortality. SLE (ICD-10 codes M32.1-M32.9) is a subset of the larger rheumatologic category and was the reason for hospitalization for only 10400 (6%) of cases. Lupus nephritis was the fifth most common reason overall for hospitalization. Patients with SLE were hospitalized for many nonlupus rheumatologic reasons, including the following diagnoses in descending order: osteoarthritis (OA) knee (codes M17.0/M17.11/M17.12), OA hip (codes M16.11/M16.12), lumbar spinal stenosis (code M48.06), cervical spinal stenosis (code M48.02), lumbar spondylolisthesis (code M43.16), and disc disorder with radiculopathy (code M51.16).

Infection category and SLE. The infectious category (ICD-10 codes A00-B99) was the third most common reason for hospitalization of patients with SLE but represented the most frequent source of in-hospital mortality. Sepsis (A41.9), pneumonia (J18.9), and urinary tract infection (N39.0) were leading infectious diagnoses. Sepsis, unspecified organism (A41.9) was both the most common reason for death and the most frequent individual principal diagnosis; it accounted for 12000 hospitalizations and 935 deaths. An expanded analysis of sepsis was done by combining the following codes: streptococcal sepsis (A40.x), other sepsis (A41.x; ie, Staphylococcus, Hemophilus influenzae, anaerobes, Escherichia coli, other gram-negative organisms), Salmonella sepsis (A02.01), Listeria sepsis (A32.7), gonococcal sepsis (A54.86), candida sepsis (B37.7), severe sepsis without septic shock (R65.20), and septic shock (R65.21). This combination of codes showed that 15720 (8.7%) hospitalizations in patients with SLE could be attributed to sepsis of some type.

## DISCUSSION

To clarify morbidity and mortality of patients with SLE on a national level, we completed a comprehensive review of SLE hospitalizations using the most recent release of the NIS database.

Prior studies of the NIS either queried for specific diagnoses of interest, examined only the most frequent diagnoses seen in patients with SLE, or limited the diagnoses reviewed (3,4,7,10-12, 15). For example, a recent analysis by Dhital et al (10) of the NIS 2016 reported on several organ/disease categories, but unfortunately many of these categories were incomplete. For example, the neurologic category failed to include strokes or neuropathies. Additionally, their methodology missed many common reasons for hospitalization, including injury and poisonings, oncologic diagnoses, endocrine diagnoses, obstetric diagnoses, psychiatric diagnoses, dermatologic diagnoses, eve and ear diagnoses, and accidents. In contrast, our methodology provides a more complete picture of SLE hospitalizations by categorizing hospitalizations and deaths by the initial three-digit stem of the seven-digit ICD-10 principal diagnosis code. This methodology has never been used for SLE in the peer-reviewed literature and thus uncovers new results. For example, gastrointestinal and respiratory diagnoses each accounted for 10% of hospitalizations, whereas injury and poisonings accounted for 9% of hospitalizations and 7% of mortality. Psychiatric, dermatologic, obstetrical, and neurologic diagnoses each accounted for only 3% of hospitalizations and had minimal mortality. Pneumonia J18.9 was the third most common principal diagnosis. Acute kidney failure N17.9 and lupus nephritis M31.24 were the fourth and fifth most common principal diagnoses, respectively, and together accounted for 6910 (4%) of hospitalizations. Despite not traditionally being associated with SLE, chronic obstructive pulmonary disease exacerbation J44.1 was the sixth most common principal diagnosis. Urinary tract infection was the 10th most common principal diagnosis.

Like prior studies, CV, rheumatologic, and infectious diagnoses were the most frequent reasons for hospitalization and together accounted for 40% of the hospitalizations in the NIS 2017. We found a high inpatient CV burden for patients with SLE. This finding is not surprising because Manzi et al previously reported that females with SLE has a 50-fold risk of MI (16). Additionally, a previous focused analysis of the NIS 1998 by Thorburn and Ward (4) found that 5% of SLE hospitalizations were for acute MI, unstable angina, cardiac catheterization, or coronary artery bypass grafting. Their numbers were smaller because they did not include all CV diagnoses, such as congestive heart failure or atrial fibrillation. Regardless, these studies emphasize the imperative that patients with SLE adhere to CV preventative strategies as one means to improve SLE outcomes.

The rheumatologic diagnoses accounted for 13% hospitalizations and were the second most common principal diagnosis category. SLE (ICD-10 codes M32.1-M32.9) itself is a subset of the larger rheumatologic principal diagnosis category (M00-M99) but only accounted for 6% of the hospitalizations. For comparison, Gu et al showed in a single-center study that active SLE was the reason for hospitalization in 21% of their cases and that, like our study, SLE was not the top reason for hospitalization (8). They reported "incidental diagnoses" as the most common reason for hospitalization. Edwards et al reported the cause of hospital admission was SLE flare in 58% of their cases (6). In a single-center study by Petri and Genovese, active lupus was described to account for 35% of the hospital admissions (14). The number of hospitalizations attributed to SLE in our study was lower than those of other studies probably because we had a nationally representative sample rather than a specialty referral hospital. Interestingly, many noninflammatory arthritic conditions were listed as principal diagnoses for patients with SLE in the NIS 2017.

The infectious category was the third most common reason for hospitalization of patients with SLE but represented the most frequent source of in-hospital mortality. Similar findings have been reported in other studies (3,5,6,8,9). Tektonidou et al queried the NIS 1996-2011 for several specific serious infections and found them to be over 12 times higher than in patients without SLE (3). In three single-center studies, 14%, 22%, and 37% of hospitalizations of patients with SLE were for infectious reasons (6,8,14). In our study, sepsis A41.9, the single most common principal diagnosis, does not specify a microorganism. Presumably, the microbiologic etiology of sepsis is unknown in the majority of cases. When specified, the etiology of sepsis was most frequently Pseudomonas, S. aureus, and gram-negative rods. We found a high burden of sepsis among SLE hospitalizations. Sepsis accounted for 8.7% of the hospitalizations and was the most common reason for death. These findings are not unexpected because infection is a welldescribed source of morbidity and mortality in SLE (3,5,8,10) due both to the immunocompromised status of patients with SLE and to the immunosuppressive therapies that they receive.

We found all-cause in-hospital mortality for patients with SLE to be 2%, which is similar to other studies (2,6,17). Krishnan found that 3.3% of SLE hospitalizations experienced in-hospital death in an analysis of the NIS from 1998 to 2002 (2). Anastasiou et al reported that the risk of inpatient death decreased from 2.2% to 1.5% (p < 0.001) among hospitalizations for patients with SLE between 2006 and 2016 in the NIS (17). Dhital et al reported an inpatient mortality of 1.96% for patients with SLE and 1.67% for matched controls (p = 0.04) in a study of the NIS 2016 (10); they also found that infectious and cardiac diagnoses were leading reasons for in-hospital mortality. None of these previous studies of the NIS comprehensively categorized the reasons for mortality. Ward reported a slightly higher in-hospital mortality of 5.1% in California during their analysis of state data from 1991 to 1994 (18). A study by Goss et al from Washington State showed that in-hospital mortality was estimated to decrease from 3.12% in 2003 to 1.28% by 2011 (p = 0.001) (19). In two smaller single-center studies, in-hospital mortality was found to be 1.4% (7 of 491) and 3.2% (11 of 348) (6,8). In summary, in-hospital mortality for patients with SLE has improved over the years but remains a serious problem. Our analysis showed that infectious and CV diagnoses together accounted for 58% of the in-hospital deaths, but other diagnoses, such as injury and poisoning deaths,

were higher than anticipated and have never been reported before in an SLE population.

The major strengths of this study include the large and representative sample size, characteristic of US hospitalizations, and the first comprehensive categorization of all SLE hospitalizations to date. This provides novel insight into the multiple comorbidities associated with SLE. Limitations include the following. First, the study relies exclusively on coding rather than clinical details, so it was not possible to verify the SLE diagnosis. Second, it was not possible to confirm the listed principal diagnosis as the actual reason for hospitalization or the actual cause of in-hospital death. NIS does not contain death certificate-level data. Third, this report reflects data on total SLE hospitalizations rather than on individual patients; individuals who were hospitalized multiple times could not be discerned. Fourth, the NIS lacks outpatient data. Fifth, analysis by broad ICD-10 diagnosis categories underrepresents the infection category. Unfortunately, not all infections are categorized in the "infection" category of ICD-10. For example, septic arthritis is categorized as a rheumatologic problem and pneumonia is categorized as a pulmonary problem.

In summary, this analysis represents the only report to date to comprehensively categorize reasons for hospitalization and in-hospital mortality of patients with SLE on a national level in the United States. A total of 180975 hospitalizations had either a principal or secondary diagnosis of SLE. The majority of the patients admitted with a diagnosis of SLE were white and female. They had an average age of 52 years and a mean LOS of 5.4 days. The mean total hospitalization charges for patients with SLE were \$61 308. SLE itself was the principal diagnosis in only 6% of the hospitalizations. We found that the overwhelming majority of both hospitalizations and deaths involving patients with SLE were for nonrheumatologic reasons. We found leading reasons for hospitalization were CV (16%), rheumatologic (13%), infectious (11%), respiratory (10%), and gastrointestinal (10%). Surprisingly, injury and poisoning accounted for 9% of hospitalizations and 7% of mortalities. In-hospital death occurred in 1 of every 50 SLE hospitalizations. Infectious diagnoses and CV diagnoses were the most common reasons for in-hospital death. Specifically, sepsis was the most frequent reason for death.

# AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual contact, and all authors approved the final version to be published. Dr. Manadan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study conception and design. Manadan, Khambhatla, Gauto-Mariotto, Okoli, Block. Acquisition of data. Manadan, Khambhatla, Gauto-Mariotto, Okoli, Block.

### REFERENCES

1. Clarke AE, Esdaile JM, Bloch DA, Lacaille D, Danoff DS, Fries JF. A Canadian study of the total medical costs for patients with systemic lupus erythematosus and the predictors of costs. Arthritis Rheum 1993;36:1548–59.

- 2. Krishnan E. Hospitalization and mortality of patients with systemic lupus erythematosus. J Rheumatol 2006;33:1770–4.
- Tektonidou MG, Wang Z, Dasgupta A, Ward MM. Burden of serious infections in adults with systemic lupus erythematosus: a national population-based study, 1996–2011. Arthritis Care Res (Hoboken) 2015;67:1078–85.
- Thorburn CM, Ward MM. Hospitalizations for coronary artery disease among patients with systemic lupus erythematosus. Arthritis Rheum 2003;48:2519–23.
- Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. Medicine (Baltimore) 2003;82:299–308.
- Edwards CJ, Lian TY, Badsha H, Teh CL, Arden N, Chng HH. Hospitalization of individuals with systemic lupus erythematosus: characteristics and predictors of outcome. Lupus 2003;12:672–6.
- Tektonidou MG, Wang Z, Ward MM. Brief report: trends in hospitalizations due to acute coronary syndromes and stroke in patients with systemic lupus erythematosus, 1996 to 2012. Arthritis Rheumatol 2016;68:2680–5.
- Gu K, Gladman DD, Su J, Urowitz MB. Hospitalizations in patients with systemic lupus erythematosus in an academic health science center. J Rheumatol 2017;44:1173–8.
- Da Rosa GP, Ortega MF, Teixeira A, Espinosa G, Cervera R. Causes and factors related to hospitalizations in patients with systemic lupus erythematosus: analysis of a 20-year period (1995–2015) from a single referral centre in Catalonia. Lupus 2019;28:1158–66.
- Dhital R, Pandey RK, Poudel DR, Oladunjoye O, Paudel P, Karmacharya P. All-cause hospitalizations and mortality in systemic lupus erythematosus in the US: results from a national inpatient database. Rheumatol Int 2020;40:393–7.
- Ando T, Adegbala O, Akintoye E, Ashraf S, Briasoulis A, Takagi H, et al. Acute myocardial infarction outcomes in systemic lupus erythematosus (from the Nationwide Inpatient Sample). Am J Cardiol 2019;123:227–32.
- Murray SG, Schmajuk G, Trupin L, Gensler L, Katz PP, Yelin EH, et al. National lupus hospitalization trends reveal rising rates of herpes zoster and declines in pneumocystis pneumonia. PLoS One 2016;11:e0144918.
- Chen SK, Barbhaiya M, Solomon DH, Guan H, Yoshida K, Feldman CH, et al. Atrial fibrillation/flutter hospitalizations among US Medicaid recipients with and without systemic lupus erythematosus. J Rheumatol 2020;47:1359–65.
- Petri M, Genovese M. Incidence of and risk factors for hospitalizations in systemic lupus erythematosus: a prospective study of the Hopkins Lupus Cohort. J Rheumatol 1992;19:1559–65.
- 15. Kishore S, Jatwani S, Malhotra B, Lirette ST, Mittal V, Vikas M. Systemic lupus erythematosus is associated with a high risk of venous thromboembolism in hospitalized patients leading to poor outcomes and a higher cost: results from Nationwide Inpatient Sample database 2003–2011. ACR Open Rheumatol 2019;1:194–200.
- Manzi S, Meilahn EN, Rairie JE, Conte CG, Medsger TA Jr, Jansen-McWilliams L, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol 1997;145:408–15.
- Anastasiou C, Trupin L, Glidden DV, Li J, Gianfrancesco M, Shiboski S, et al. Mortality among hospitalized individuals with systemic lupus erythematosus in the United States between 2006 and 2016. Arthritis Care Res (Hoboken) 2020. E-pub ahead of print. https:// orcid.org/10.1002/acr.24356

2002;29:1198-206.

- 18. Ward MM. Hospital experience and mortality in patients with systemic lupus erythematosus: which patients benefit most from treatment at highly experienced hospitals? [comparative study]. J Rheumatol
  - Goss LB, Ortiz JR, Okamura DM, Hayward K, Goss CH. Significant reductions in mortality in hospitalized patients with systemic lupus erythematosus in Washington State from 2003 to 2011. PLoS One 2015;10:e0128920.