Trends, outcomes, and disparities in hospitalizations among patients with Sjögren's syndrome: a national inpatient sample analysis (2016–2020)

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Running title: Sjögren's syndrome hospitalization outcomes

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Submitted: 21/03/2026

Accepted: 07/06/2026

ABSTRACT

Aims: Sjögren's syndrome (SS) is a systemic autoimmune disease with poorly characterized hospitalization outcomes in the United States. We aimed to characterize hospitalization trends, comorbidity profiles, organ-specific manifestations, predictors of in-hospital mortality, and racial, socioeconomic, and hospital-level disparities among SS-associated hospitalizations using the NIS 2016–2020 dataset.

Methods: Retrospective cross-sectional analysis of the NIS (2016–2020). Adults with SS (ICD-10-CM M35.00–M35.0C) were identified across 40 diagnosis fields and matched 3:1 with non-autoimmune controls by age, sex, and year. Survey-weighted analyses included bivariate comparisons, Elixhauser comorbidity profiling, organ-specific phenotyping, nested multivariable logistic regression for mortality predictors, and adjusted disparities analyses using predictive margins.

Results: Among 272,630 weighted SS-associated hospitalizations (91.4% female, mean age 64.2 years), extraglandular manifestations were documented in 33.8%. Despite a significantly higher baseline comorbidity burden compared with 817,890 matched control hospitalizations, SS-associated admissions exhibited paradoxically lower crude in-hospital mortality (2.13% vs. 2.59%, p<0.001). However, within the SS cohort, acute complications were associated with substantial mortality risk in the fully adjusted model: independent predictors included mechanical ventilation (OR 21.08), sepsis (OR 2.80), stroke (OR 2.78), malignancy (OR 2.46), and interstitial lung disease (OR 2.10). Significant disparities persisted after multivariable adjustment: Asian/Pacific Islander hospitalizations had higher mortality odds (OR 1.67, p=0.002) and incurred $22,643 more in adjusted charges compared with White hospitalizations. Self-pay or uninsured status was associated with doubled mortality odds (OR 2.01, p<0.001).

Conclusions: Enhanced clinical phenotyping underscores that Sjögren's syndrome is a complex, multisystem disease with a substantial inpatient burden. While SS-associated hospitalizations present with high baseline comorbidities, in-hospital mortality is strongly associated with acute complications, particularly respiratory failure, sepsis, stroke, and interstitial lung disease. Future clinical pathways should prioritize vigilant management of these vulnerabilities while addressing the structural and socioeconomic disparities associated with unequal outcomes.

Keywords: Sjogren's Syndrome; Hospitalization; Outcome Measures; Health Economics; Risk Factors.

INTRODUCTION

Sjögren's syndrome (SS) is a prevalent systemic autoimmune disease characterized by exocrine gland dysfunction classically presenting as xerostomia and keratoconjunctivitis sicca alongside a complex spectrum of extraglandular manifestations. Affecting up to 4.8% of the population with a striking 9:1 female predominance, SS may present independently as a primary disease or secondary to other connective tissue disorders, most notably rheumatoid arthritis and systemic lupus erythematosus[1].

Historically mischaracterized as a predominantly benign glandular disorder, SS is increasingly recognized for its profound systemic morbidity. Extraglandular manifestations, including interstitial lung disease, renal tubular acidosis, peripheral neuropathy, and a well-established risk of non-Hodgkin lymphoma, frequently precipitate severe clinical deterioration and hospital admission[2]. Despite this considerable disease burden, population-level data characterizing hospitalization trends, clinical outcomes, and health disparities among patients with SS remain notably sparse. Prior foundational studies evaluating national inpatient data were constrained by the limited coding specificity of the ICD-9 era, often precluding detailed organ-specific phenotyping or the assessment of mortality predictors. The transition to the ICD-10-CM coding system in October 2015 marked a pivotal advancement, introducing granular diagnostic codes for specific SS phenotypes, such as keratoconjunctivitis sicca, lung involvement, tubulo-interstitial nephropathy and other organ-specific manifestations. Leveraging the complete five-year window of ICD-10-coded data from the National Inpatient Sample (NIS), this study aims to provide a comprehensive evaluation of outcomes in SS-associated hospitalizations to date.

MATERIAL AND METHODS

Study Design and Data Source

This was a retrospective cross-sectional study utilizing the NIS database for the years 2016 through 2020. The NIS is the largest publicly available all-payer inpatient healthcare database in the United States, maintained by the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ). Since the 2012 redesign, the NIS contains data from a 20% stratified sample of all discharges from community hospitals nationwide, representing approximately 35 million hospitalizations annually when discharge-level weights are applied. The NIS includes up to 40 ICD-10-CM diagnosis codes and 25 ICD-10-PCS procedure codes per discharge. Since the NIS contains de-identified data, this study was exempt from Institutional Review Board approval[3].

Study Population

All adult hospitalizations (≥18 years) with a diagnosis of SS in any of the 40 diagnosis fields were identified using ICD-10-CM codes M35.00 through M35.0C. All clinical manifestations, comorbidities, and complications were ascertained exclusively from ICD-10-CM diagnosis codes; no clinical record review was performed. A matched control group of hospitalizations was constructed, drawing from adult admissions without any autoimmune disease diagnosis. Control hospitalizations were frequency-matched 3:1 to SS-associated hospitalizations based on 5-year age bins, sex, and discharge year. The unit of analysis throughout was the individual hospitalization, not the unique patient.

Study Variables

Discharge-level demographic variables included age, sex, race/ethnicity, primary payer, and median household income quartile. Hospital characteristics included bed size, teaching status, and region. Comorbidity burden was quantified using the AHRQ Elixhauser Comorbidity Index 4. Organ-specific SS manifestations were classified using ICD-10-CM codes, including pulmonary involvement (interstitial lung disease, pulmonary arterial hypertension, pleural disease), renal involvement, central and peripheral nervous system involvement, cutaneous vasculitis, and hematologic involvement. In-hospital complications included infections (sepsis, bacterial pneumonia, COVID-19, urinary tract infection, fungal infection), cardiovascular events (acute myocardial infarction, stroke, atrial fibrillation, venous thromboembolism, heart failure), acute

kidney injury, and malignancies (with lymphoma and MALT lymphoma analyzed separately). Procedures included mechanical ventilation and hemodialysis.

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included length of stay (LOS), total hospital charges, and discharge disposition.

Statistical Analysis

All analyses incorporated NIS survey design elements, including discharge-level weights, hospital-level clustering, and stratification, using Stata version 19 (StataCorp, College Station, TX). The analysis comprised two distinct components. First, comparative analyses evaluated differences between SS-associated and control hospitalizations in baseline characteristics, comorbidity profiles, and complication rates. Baseline characteristics were compared using Rao-Scott chi-square tests (categorical) and survey-weighted t-tests (continuous) [5]. Comorbidity comparisons used survey-weighted logistic regression adjusted for race, hospital teaching status, insurance, and income. Second, within-cohort analyses restricted to SS-associated hospitalizations examined predictors of in-hospital mortality, health disparities, and temporal trends; these within-cohort models were not applied to the control group. Predictors of mortality were identified using a nested multivariable logistic regression approach: Model 1 (demographics, comorbidity burden, hospital characteristics), Model 2 (Model 1 plus organ-specific involvement), Model 3 (Model 1 plus acute complications and procedures), and Model 4 (full model). Disparities were evaluated using separate adjusted logistic (mortality) and linear (LOS, charges) regression models with predictive margins [6]. Temporal trends were assessed using discharge year as a continuous predictor. Sensitivity analyses included restriction to non-elective admissions (S1); restriction to hospitalizations with SS listed as the principal diagnosis (S2); an approximate primary SS subgroup (S3), constructed by screening all 40 ICD-10-CM diagnosis fields and excluding hospitalizations with concurrent codes for rheumatoid arthritis (M05, M06), systemic lupus erythematosus (M32), systemic sclerosis (M34), dermatomyositis/polymyositis (M33), or mixed connective tissue disease (M35.1); age-stratified models (<65 and ≥65 years; S4); and exclusion of the pandemic year 2020 (S5). A two-sided $p<0.05$ was considered significant.

RESULTS

Study Population and Baseline Characteristics

A total of 54,526 unweighted hospitalizations with SS were identified, representing 272,630 weighted discharges nationally. These were matched to 163,578 control hospitalizations (817,890 weighted), yielding 218,104 analytical records. The SS cohort was predominantly female (91.38%) with a mean age of 64.21 years. Compared with control hospitalizations, SS-associated admissions were more frequently among White individuals (74.55% vs. 67.55%), privately insured or Medicare-covered, from higher-income zip codes (Q4: 26.59% vs. 19.37%), and treated at urban teaching hospitals (74.25% vs. 68.81%). SS-associated hospitalizations had substantially greater comorbidity burden, with 50.81% having ≥5 Elixhauser comorbidities versus 33.41% in controls ($p<0.001$). Mean LOS was 5.10 days and mean charges were $62,839. Notably, despite this higher comorbidity burden, crude in-hospital mortality was paradoxically lower among SS-associated hospitalizations than matched control hospitalizations (2.13% vs. 2.59%, $p<0.001$) (Table I).

Comorbidity Profile: SS-Associated vs. Control Hospitalizations

Compared with matched control hospitalizations, SS-associated admissions demonstrated significantly elevated odds of lymphoma (adjusted OR 2.19, 95% CI 1.97–2.43), hypothyroidism (OR 1.83, 95% CI 1.78–1.89), pulmonary circulation disorders (OR 1.84, 95% CI 1.74–1.94), congestive heart failure (OR 1.44, 95% CI 1.39–1.49), chronic pulmonary disease (OR 1.34, 95% CI 1.30–1.39), depression (OR 1.25, 95% CI 1.20–1.29), and valvular disease (OR 1.31, 95% CI 1.26–1.37) (Table II). Conversely, SS-associated hospitalizations had significantly lower odds of uncomplicated diabetes (OR 0.69), complicated diabetes (OR 0.68), obesity (OR 0.83), alcohol abuse (OR 0.50), and drug abuse (OR 0.52; all $p<0.001$) (Table II).

Organ Involvement and Complications: SS-Associated vs. Control Hospitalizations

Extraglandular manifestations were documented in 33.81% of SS-associated hospitalizations. The most frequent organ involvements were peripheral neuropathy (8.21%), pulmonary arterial hypertension (7.77%), and interstitial lung disease (7.14%). Compared with control hospitalizations, SS-associated admissions had markedly higher rates of ILD (OR 8.68, 95% CI 7.99–9.43), ocular complications (OR 5.83, 95% CI 5.14–6.62), cutaneous vasculitis (OR 4.45, 95% CI 3.79–5.22), and peripheral neuropathy (OR 2.71, 95% CI 2.56–2.86). MALT lymphoma, though rare (0.19%), showed the highest OR at 15.76 (95% CI 9.18–27.05). Infections were present in

29.10% of SS-associated admissions, with sepsis (10.77%), bacterial pneumonia (10.62%), and urinary tract infections (10.31%) being the most common. Heart failure (18.26%), atrial fibrillation (15.99%), and acute kidney injury (15.91%) were prevalent cardiovascular/renal complications (Table III).

Predictors of In-Hospital Mortality Among SS-Associated Hospitalizations

Among SS-associated hospitalizations, non-survivors were significantly older (71.36 vs. 64.05 years), more frequently male, and had higher comorbidity burden (mean Elixhauser 6.46 vs. 4.70; all p<0.001) (Table IV). In the fully adjusted multivariable model restricted to the SS cohort (Table V), the strongest independent predictor of mortality was mechanical ventilation (OR 21.08, 95% CI 17.40–25.55), followed by sepsis (OR 2.80, 95% CI 2.30–3.40), stroke (OR 2.78, 95% CI 2.19–3.53), malignancy (OR 2.46, 95% CI 2.09–2.89), and ILD (OR 2.10, 95% CI 1.74–2.53). AKI (OR 1.92), dialysis (OR 1.78), AMI (OR 1.60), VTE (OR 1.59), and heart failure (OR 1.25) were also significant. Notably, renal involvement became protective in the full model (OR 0.49, 95% CI 0.37–0.65), suggesting that the most common SS renal manifestation (tubular acidosis) identifies a less acutely ill phenotype once complications are controlled (Tables IV, V).

Sequential nested model construction (Supplementary Table S1) revealed that the Elixhauser ≥5 OR decreased from 12.64 in the demographics-only model to 3.61 in the full model, demonstrating that the comorbidity–mortality association is largely mediated through specific acute complications rather than comorbidity burden per se.

Health Disparities Among SS-Associated Hospitalizations

After adjustment for age, sex, insurance, and comorbidity burden, significant racial disparities persisted among SS-associated hospitalizations. Asian/Pacific Islander hospitalizations had the highest adjusted mortality (OR 1.67, 95% CI 1.20–2.31, p=0.002), followed by Hispanic (OR 1.34, 95% CI 1.07–1.67, p=0.010) and Black hospitalizations (OR 1.24, 95% CI 1.01–1.51, p=0.036). Charge disparities were even more pronounced: Asian/Pacific Islander hospitalizations incurred $22,643 more (p<0.001) and Hispanic hospitalizations $19,681 more (p<0.001) in adjusted charges compared with White hospitalizations (Table VI).

Insurance status, hospital characteristics, and regional variation also influenced outcomes (Supplementary Table S2). Self-pay/other insurance was associated with doubled mortality odds compared with Medicare (OR 2.01, p<0.001). Urban teaching hospitals charged $31,634 more than rural hospitals despite similar adjusted mortality rates. The West region charged $15,458 more than the Northeast (p<0.001), while income quartile was not significantly associated with mortality after adjustment.

Temporal Trends

Weighted SS hospitalizations ranged from 49,005 (2016) to 60,315 (2019), declining to 54,040 in 2020. In-hospital mortality increased from 1.93% (2016) to 2.57% (2020; trend OR 1.050 per year, p=0.024). Mean charges rose from $54,711 to $71,439. AKI showed a significant upward trend (OR 1.060 per year, p<0.001). The proportion with SS as principal diagnosis declined from 0.84% to 0.52%, and 95.93% carried the unspecified code M35.00.

Sensitivity Analyses

Five pre-specified sensitivity analyses confirmed the robustness of the primary findings. Restriction to non-elective admissions only (n=42,747; 78.4% of the cohort) produced effect estimates closely comparable to the full cohort: mechanical ventilation OR 24.36 (vs. 21.08 in the primary analysis), sepsis OR 2.47 (vs. 2.80), and age ≥75 OR 5.46 (vs. 5.43), indicating that the inclusion of lower-acuity elective admissions does not materially attenuate mortality predictors.

To address the potential confounding influence of overlapping connective tissue diseases, an approximate primary SS subgroup was constructed by systematically screening all 40 ICD-10-CM diagnosis fields for concurrent codes for rheumatoid arthritis (M05, M06), systemic lupus erythematosus (M32), systemic sclerosis (M34), dermatomyositis/polymyositis (M33), and mixed connective tissue disease (M35.1). Hospitalizations carrying any of these codes were excluded, yielding 32,658 hospitalizations (59.97% of the SS cohort) without documented overlap with other major connective tissue diseases. The full multivariable mortality model was then re-estimated in this restricted subgroup, producing effect estimates that were qualitatively similar to the primary analysis across all key predictors, including mechanical ventilation, sepsis, ILD, and extraglandular involvement. A separate restriction to hospitalizations listing SS as the principal diagnosis identified only approximately 162 records, precluding reliable multivariable modeling and confirming that SS is overwhelmingly coded as a secondary diagnosis in the inpatient setting. Age-stratified analyses revealed meaningful differences in effect sizes: among hospitalizations in patients younger than 65 years, sepsis carried a notably higher OR (5.36 vs. 4.06 in ≥65) and extraglandular involvement was a stronger predictor (OR 1.90 vs. 1.32). Exclusion of the pandemic-influenced year 2020 (n=43,660) demonstrated stable effect estimates (mechanical ventilation OR 24.07, age ≥75 OR 7.89), confirming that the primary findings are not confounded by COVID-19-era changes in hospitalization patterns or case mix.

DISCUSSION

This study presents an analysis of outcomes among SS-associated hospitalizations in the United States, leveraging the enhanced clinical granularity of ICD-10 coding across 54,526 hospitalizations over five years. An important finding was that crude in-hospital mortality was paradoxically lower among SS-associated hospitalizations than matched controls (2.13% vs. 2.59%, p<0.001), despite SS-associated admissions carrying a substantially higher coded comorbidity burden. This finding is likely explained by several complementary mechanisms. First, admission threshold bias may play a role: patients with SS are typically followed by rheumatologists and may be hospitalized at a lower acuity threshold for disease flares, diagnostic evaluations, infusion therapy, or elective procedures, as compared with control hospitalizations that may more frequently represent acute illness. The elevated Elixhauser scores in SS-associated admissions are driven predominantly by chronic conditions (hypothyroidism, chronic pulmonary disease, depression, rheumatoid arthritis) that carry diagnostic codes without necessarily conferring acute mortality risk. In contrast, the general hospitalized control population includes acute surgical emergencies, trauma, decompensated organ failure, and advanced malignancies with inherently higher short-term lethality. Second, differential coding practices in high-acuity settings may contribute: in severely ill patients, chronic conditions such as SS may be undercoded if not directly relevant to the acute admission, potentially leading to misclassification of the most acutely ill SS patients into the control group and further depressing the observed crude mortality rate in the SS cohort. Third, the SS cohort's demographic profile—predominantly female, higher income, and concentrated in urban teaching hospitals—confers baseline prognostic advantages not fully captured by age-sex-year matching alone. This apparent paradox extends to the acute complications themselves. Compared with matched controls, SS-associated hospitalizations exhibited lower crude rates of mechanical ventilation, stroke, acute myocardial infarction (AMI), and overall malignancy. Rather than indicating a disease-specific protective effect, this pattern likely reflects the demographic composition of the SS cohort, which carries a lower baseline burden of traditional cardiometabolic risk factors such as diabetes and substance use. However, when these acute events do occur within the SS population, they are associated with substantial mortality risk.

Mechanical ventilation emerged as the dominant predictor (OR 21.08), consistent with the known severity of respiratory failure in autoimmune conditions[7]. Sepsis (OR 2.80) is a particularly noteworthy finding, as patients with SS may face increased infection risk due to both

immunological dysfunction and immunosuppressive therapy[8]. The role of ILD as an independent predictor (OR 2.10) aligns with its recognition as a major determinant of morbidity in SS [9]. The observed prevalence of pulmonary arterial hypertension (7.77%) among SS-associated hospitalizations merits comment, as this rate exceeds what might be expected for primary SS alone. This likely reflects, in part, the contribution of overlapping connective tissue diseases, particularly systemic sclerosis, which carries a well-established high prevalence of pulmonary hypertension as well as the broad capture of pulmonary circulation disorders by the ICD-10-CM coding used in this analysis. Notably, the sensitivity analysis restricted to approximate primary SS (excluding overlapping connective tissue diseases) produced consistent overall findings (Supplementary Table S3), though the relative contribution of overlap conditions to specific organ manifestations such as PAH cannot be fully quantified in administrative data.

An important consideration is whether mortality predictors differ when SS is the primary reason for admission versus a secondary comorbidity complicating another acute process. In our cohort, SS was listed as the principal diagnosis in fewer than 1% of hospitalizations (declining from 0.84% in 2016 to 0.52% in 2020), consistent with the 1.3% reported by Koch et al. and the pattern described by Domańska-Poboza *et al.* in Poland, where 70.3% of SS hospitalizations carried M35.0 as the primary code but the vast majority were planned diagnostic admissions[10,11]. When we restricted our mortality model to principal-diagnosis-only SS cases (n=162 unweighted), the sample was too small for reliable multivariable modeling, with wide confidence intervals precluding meaningful effect estimation. This underpowered result is itself informative: it underscores that SS rarely drives the acute admission itself, and that most SS-associated in-hospital mortality occurs in the context of SS as a background comorbidity complicating other primary conditions such as sepsis, cardiovascular events, respiratory failure, or malignancy. The clinical implication is that the mortality risk among hospitalized patients with SS may relate less to the autoimmune disease per se and more to the systemic vulnerability it may confer: immunological dysfunction that may predispose to infection, chronic inflammation that may accelerate multisystem disease, and immunosuppressive therapy that may compound both risks. This distinction has practical importance for inpatient management, as it suggests that vigilant monitoring for sepsis, respiratory decompensation, and acute kidney injury should be prioritized in any hospitalized SS patient, regardless of the primary admission diagnosis. Future studies using clinical registries that capture SS disease activity scores (ESSDAI) alongside hospitalization data would be better positioned to disentangle the contributions of disease-specific flares from background systemic vulnerability[8].

The racial and socioeconomic disparities identified in this study are novel for SS. Asian/Pacific Islander patients faced 67% higher adjusted mortality, while Hispanic patients had 34% higher odds and Black patients 24% higher odds compared with White patients. These disparities persisted after adjustment for age, sex, insurance, and comorbidity burden, suggesting that unmeasured factors including access to rheumatologic subspecialty care, disease recognition and diagnostic delays, language barriers, and structural racism may contribute[12,13]. The charge disparities were even more striking, with Asian/Pacific Islander and Hispanic patients incurring approximately $20,000 more than White patients, potentially reflecting more advanced disease at presentation or differential treatment patterns.

The rising mortality trend (OR 1.050 per year, p=0.024) warrants investigation. While the 2020 data may reflect COVID-19's direct and indirect effects, exclusion of 2020 did not fully attenuate this trend. Possible explanations include increasing disease severity at presentation and rising prevalence of multimorbidity in an aging population.

Our study has several limitations inherent to administrative data analysis. First, the NIS relies on ICD-10-CM coding rather than validated classification criteria such as the 2016 ACR/EULAR criteria. This introduces potential misclassification bias, and all clinical phenotyping including organ-specific manifestations was derived exclusively from diagnostic codes, not from clinical record review, which may affect the accuracy of phenotypic characterization. Second, the NIS does not contain autoantibody profiles (anti-Ro/SSA, anti-La/SSB), serologic markers, salivary gland biopsy results, or disease activity scores (ESSDAI), all of which are relevant to disease severity and prognosis. Third, medication data are not available in the NIS; therefore, the influence of immunosuppressive therapies on outcomes including medication-related infection risk, treatment-related complications, and differences in disease control could not be assessed. This limitation is particularly relevant given that sepsis emerged as a strong independent mortality predictor, as the contribution of immunosuppressive therapy to infection susceptibility cannot be disentangled from the effects of the disease itself. Fourth, we could not reliably distinguish primary from secondary SS; our proxy exclusion of overlapping connective tissue diseases provides only an approximation. A substantial proportion of SS-associated hospitalizations had coexisting rheumatoid arthritis (30.44%), SLE, or systemic sclerosis, which may independently influence hospitalization risk and mortality. However, the sensitivity analysis restricted to the approximate primary SS subgroup (excluding all overlapping connective tissue diseases) yielded consistent effect estimates across all key mortality predictors (Supplementary

Table S3), suggesting that the core findings are not driven by secondary SS. Fifth, as the NIS captures hospitalizations rather than unique patients, some individuals may contribute multiple admissions, and the same patient cannot be tracked over time. Sixth, the NIS captures only in-hospital mortality; out-of-hospital mortality was not assessed, which may lead to underestimation of the true mortality burden associated with the disease. Seventh, the 2020 data may be influenced by pandemic-related changes in healthcare utilization and coding practices, though the sensitivity analysis excluding 2020 produced stable findings. Finally, coding practices in high-acuity hospitalizations may contribute to the observed mortality paradox: in severely ill patients, chronic conditions such as SS may be undercoded if not directly relevant to the admission, potentially leading to misclassification into the control group. Despite these limitations, the NIS provides statistical power and national representativeness for examining hospitalization outcomes and disparities that cannot be achieved with single-center or registry-based designs.

CONCLUSIONS

This nationally representative analysis of over 272,000 SS-associated hospitalizations underscores that Sjögren's syndrome is a systemic disease with substantial inpatient morbidity. By leveraging the enhanced clinical phenotyping of the ICD-10 era, we demonstrate that while SS-associated hospitalizations present with high chronic comorbidity burden, in-hospital mortality is strongly associated with acute complications, particularly respiratory failure, sepsis, stroke, and interstitial lung disease. These findings suggest that underlying immune dysregulation, chronic inflammation, and systemic organ involvement may compromise physiological reserve during acute insults.

Our analysis also reveals notable racial, ethnic, and socioeconomic disparities in both clinical outcomes and healthcare utilization among SS-associated hospitalizations. The elevated mortality odds and hospital charges observed among Asian/Pacific Islander, Hispanic, Black, and uninsured hospitalizations highlight important inequities that warrant further investigation. Future efforts should prioritize addressing these disparities, optimizing the acute management of infectious and respiratory complications in hospitalized patients with SS, and furthering the recognition of Sjögren's syndrome as a systemic disease with significant inpatient implications.

Tables and Figures

Table I. Baseline Characteristics of Hospitalized Patients with Sjögren's Syndrome and Matched Controls

Characteristic	Sjögren's Syndrome (n = 272,630)	Matched Controls (n = 817,890)	P-value
Weighted N	272,630	817,890	
Unweighted N	54,526	163,578	
Demographics			
Age, mean (SD)	64.21	64.20	0.966
18–39 years	8.85	8.85	
40–54 years	15.43	15.43	
55–64 years	20.79	20.79	
65–74 years	27.25	27.25	
≥75 years	27.67	27.67	
Female sex, %	91.38	91.38	
Race/Ethnicity, %			
White	74.55	67.55	
Black	10.10	14.43	
Hispanic	7.66	9.48	
Asian/Pacific Islander	2.38	2.58	
Native American	0.45	0.52	
Other	4.87	5.44	<0.001
Primary payer, %			
Medicare	63.17	58.13	
Medicaid	7.42	13.10	
Private insurance	26.27	23.58	
Self-pay/Other	3.14	5.19	<0.001
Median household income quartile, %			
Q1 (lowest)	21.92	30.61	
Q2	24.18	25.36	
Q3	27.31	24.66	
Q4 (highest)	26.59	19.37	<0.001
Hospital characteristics, %			
Urban teaching	74.25	68.81	
Urban non-teaching	18.91	21.93	
Rural	6.84	9.26	<0.001
Small bedsize	13.92	14.98	
Medium bedsize	26.08	26.93	
Large bedsize	60.00	58.09	0.003
Hospital region, %			
Northeast	21.04	18.36	
Midwest	22.16	21.45	
South	36.58	40.47	
West	20.22	19.72	<0.001
Elixhauser comorbidity burden			
0 comorbidities, %	0.00	9.33	
1–2 comorbidities, %	16.26	25.78	
3–4 comorbidities, %	32.93	31.47	

≥5 comorbidities, %	50.81	33.41	<0.001
Mean Elixhauser count	4.74	3.60	<0.001
Clinical outcomes			
In-hospital mortality, %	2.13	2.59	<0.001
Length of stay, mean days	5.10	4.91	<0.001
Total charges, mean ($)	62,839	59,991	<0.001
Routine discharge, %	56.90	57.19	
Home health care, %	18.77	17.55	
Transfer/SNF, %	19.50	18.45	0.004

NIS, National Inpatient Sample; SNF, skilled nursing facility; Q, quartile. Values are survey-weighted percentages unless otherwise specified.

Table II. Elixhauser Comorbidity Comparison: Sjögren's Syndrome vs. Matched Controls

Elixhauser Comorbidity	SS (%)	Controls (%)	OR (95% CI)	P-value	Dir.
Congestive heart failure	17	13	1.44 (1.39–1.49)	<0.001	↑
Cardiac arrhythmias	23	20	1.17 (1.13–1.21)	<0.001	↑
Valvular disease	10.14	7.91	1.31 (1.26–1.37)	<0.001	↑
Pulmonary circulation disorders	7.65	4.31	1.84 (1.74–1.94)	<0.001	↑
Peripheral vascular disorders	10.38	8.78	1.20 (1.15–1.26)	<0.001	↑
Hypertension, uncomplicated	35.66	38.91	0.87 (0.85–0.90)	<0.001	↓
Hypertension, complicated	19.81	18.34	1.10 (1.06–1.14)	<0.001	↑
Paralysis	2.65	3.16	0.83 (0.77–0.90)	<0.001	↓
Other neurological disorders	8.08	7.60	1.07 (1.02–1.12)	0.005	↑
Chronic pulmonary disease	22.11	17.49	1.34 (1.30–1.39)	<0.001	↑
Diabetes, uncomplicated	13.03	17.69	0.69 (0.67–0.72)	<0.001	↓
Diabetes, complicated	8.52	12.09	0.68 (0.65–0.71)	<0.001	↓
Hypothyroidism	23.54	14.39	1.83 (1.78–1.89)	<0.001	↑
Renal failure	15.97	16.18	0.98 (0.95–1.02)	0.367	—
Liver disease	5.52	5.38	1.03 (0.97–1.09)	0.361	—
Peptic ulcer disease	0.13	0.09	1.45 (0.96–2.19)	0.08	—
Lymphoma	2.24	1.04	2.19 (1.97–2.43)	<0.001	↑
Metastatic cancer	2.55	3.88	0.65 (0.60–0.70)	<0.001	↓
Solid tumor w/o metastasis	4.55	5.68	0.79 (0.75–0.84)	<0.001	↓
Rheumatoid arthritis/collagen	30.44	3.64	11.56 (11.05–12.09)	<0.001	↑
Coagulopathy	7.52	6.49	1.17 (1.12–1.23)	<0.001	↑
Obesity	12.48	14.59	0.83 (0.80–0.86)	<0.001	↓
Weight loss	5.78	5.75	1.01 (0.95–1.06)	0.838	—
Fluid and electrolyte disorders	24.85	22.89	1.11 (1.08–1.15)	<0.001	↑
Blood loss anemia	2.42	2.71	0.89 (0.83–0.96)	0.003	↓
Deficiency anemia	13.04	11.51	1.15 (1.11–1.20)	<0.001	↑
Alcohol abuse	1.82	3.55	0.50 (0.46–0.55)	<0.001	↓
Drug abuse	1.99	3.77	0.52 (0.47–0.57)	<0.001	↓
Psychoses	2.73	3.78	0.71 (0.66–0.77)	<0.001	↓
Depression	14.77	12.20	1.25 (1.20–1.29)	<0.001	↑

Abbreviations: SS, Sjögren's syndrome; OR, odds ratio; CI, confidence interval; Dir., direction. ↑ = higher in SS, ↓ = lower in SS, — = not significant. Survey-weighted logistic regression.

Table III. Organ Involvement, Complications, and Procedures: Sjögren's Syndrome vs. Matched Controls

Clinical Feature	SS (%)	Controls (%)	OR (95% CI)	P-value
Organ Involvement				
Extraglandular manifestations	33.81	—	—	
Interstitial lung disease	7.14	0.88	8.68 (7.99–9.43)	<0.001
Pulmonary arterial hypertension	7.77	4.36	1.85 (1.75–1.96)	<0.001
Pleural involvement	3.32	2.68	1.25 (1.16–1.35)	<0.001
Renal involvement	5.47	4.73	1.17 (1.10–1.24)	<0.001
CNS involvement	5.75	4.69	1.24 (1.17–1.32)	<0.001
Peripheral neuropathy	8.21	3.20	2.71 (2.56–2.86)	<0.001
Cutaneous vasculitis	1.40	0.32	4.45 (3.79–5.22)	<0.001
Hematologic involvement	2.64	1.57	1.70 (1.55–1.86)	<0.001
Ocular complications	2.61	0.46	5.83 (5.14–6.62)	<0.001
Arthritis/arthropathy	13.35	5.02	2.92 (2.81–3.04)	<0.001
Infectious Complications				
Any infection	29.10	25.51	1.20 (1.16–1.23)	<0.001
Sepsis	10.77	9.41	1.16 (1.11–1.21)	<0.001
Bacterial pneumonia	10.62	8.51	1.28 (1.22–1.33)	<0.001
Urinary tract infection	10.31	9.40	1.11 (1.06–1.16)	<0.001
Fungal infection	3.76	2.35	1.63 (1.52–1.75)	<0.001
COVID-19	0.93	0.85	1.10 (0.94–1.28)	0.223
Malignancies				
Lymphoma	2.32	1.08	2.18 (1.96–2.42)	<0.001
MALT lymphoma	0.19	0.01	15.76 (9.18–27.05)	<0.001
Any malignancy	8.57	10.65	0.79 (0.75–0.82)	<0.001
Cardiovascular/Renal				
Acute MI	3.23	3.81	0.84 (0.79–0.90)	<0.001
Stroke	2.34	3.06	0.76 (0.70–0.82)	<0.001
Atrial fibrillation	15.99	14.07	1.16 (1.12–1.20)	<0.001
VTE	3.27	2.74	1.20 (1.12–1.28)	<0.001
Heart failure	18.26	13.30	1.46 (1.41–1.51)	<0.001
Acute kidney injury	15.91	14.44	1.12 (1.08–1.16)	<0.001
Procedures				
Mechanical ventilation	2.94	3.18	0.92 (0.85–1.00)	0.044
Dialysis	1.76	1.68	1.05 (0.95–1.16)	0.352

Abbreviations: SS, Sjögren's syndrome; OR, odds ratio; CI, confidence interval; MI, myocardial infarction; CNS, central nervous system; MALT, mucosa-associated lymphoid tissue; VTE, venous thromboembolism. Survey-weighted logistic regression.

Table IV. Comparison of Survivors and Non-Survivors Among Hospitalized Sjögren's Syndrome Patients

Characteristic	Survived (%)	Died (%)	P-value
Demographics			
Female	97.96	2.04	
Male	96.87	3.13	<0.001
Age 18–39	99.46	0.54	
Age 40–54	98.93	1.07	
Age 55–64	98.34	1.66	
Age 65–74	97.58	2.42	
Age ≥75	96.69	3.31	<0.001
Comorbidity Burden			
Elixhauser 1–2	99.77	0.23	
Elixhauser 3–4	98.99	1.01	
Elixhauser ≥5	96.53	3.47	<0.001
Key Organ Involvement			
ILD	94.63	5.37	<0.001
PAH	95.11	4.89	<0.001
Extraglandular	96.78	3.22	<0.001
Hematologic	96.04	3.96	<0.001
Key Complications			
Sepsis	90.72	9.28	<0.001
Bacterial pneumonia	93.72	6.28	<0.001
COVID-19	89.78	10.22	<0.001
Any malignancy	95.63	4.37	<0.001
AMI	93.13	6.87	<0.001
Stroke	92.95	7.05	<0.001
Heart failure	95.55	4.45	<0.001
AKI	93.46	6.54	<0.001
Mech. ventilation	66.29	33.71	<0.001
Dialysis	89.25	10.75	<0.001
Continuous Variables (mean: survivors vs. non-survivors)			
Age, years	64.05	71.36	<0.001
Length of stay, days	5.04	8.26	<0.001
Total charges ($)	61,254	135,861	<0.001
Elixhauser count	4.70	6.46	<0.001

Overall in-hospital mortality: 2.13%. P-values from survey-weighted chi-square (categorical) or t-tests (continuous). For continuous variables, columns show mean for survivors and non-survivors respectively.

Table V. Independent Predictors of In-Hospital Mortality Among Sjögren's Syndrome Patients: Full Multivariable Model

Predictor	Adjusted OR (95% CI)	P-value
Demographics		
Age 40–54 (ref: 18–39)	1.55 (0.73–3.27)	0.25
Age 55–64	1.98 (0.97–4.06)	0.06
Age 65–74	3.46 (1.70–7.05)	<0.001
Age ≥75	5.43 (2.67–11.04)	<0.001
Female sex	0.84 (0.71–0.99)	0.04
Black (ref: White)	1.11 (0.89–1.40)	0.36
Hispanic	1.21 (0.94–1.57)	0.14
Asian/Pacific Islander	1.64 (1.14–2.35)	0.01
Insurance (ref: Medicare)		
Medicaid	1.28 (0.92–1.77)	0.14
Private	1.47 (1.19–1.81)	<0.001
Self-pay/Other	1.95 (1.44–2.63)	<0.001
Comorbidity burden (ref: Elixhauser 1–2)		
Elixhauser 3–4	2.34 (1.34–4.10)	0.00
Elixhauser ≥5	3.61 (2.09–6.24)	<0.001
Hospital		
Medium bedsize (ref: small)	1.40 (1.04–1.87)	0.02
Large bedsize	1.37 (1.04–1.81)	0.03
Organ-specific involvement		
Interstitial lung disease	2.10 (1.74–2.53)	<0.001
Pulmonary arterial hypertension	1.41 (1.15–1.73)	0.00
Renal involvement	0.49 (0.37–0.65)	<0.001
CNS involvement	0.96 (0.72–1.27)	0.77
PNS involvement	0.76 (0.57–1.01)	0.06
Hematologic involvement	1.16 (0.86–1.57)	0.33
Acute complications and procedures		
Any infection	1.37 (1.13–1.66)	0.00
Sepsis	2.80 (2.30–3.40)	<0.001
Any malignancy	2.46 (2.09–2.89)	<0.001
Lymphoma	0.69 (0.46–1.03)	0.07
Acute myocardial infarction	1.60 (1.25–2.05)	<0.001
Stroke	2.78 (2.19–3.53)	<0.001
Venous thromboembolism	1.59 (1.21–2.10)	0.001
Heart failure	1.25 (1.06–1.48)	0.008
Valvular disease	0.85 (0.67–1.08)	0.179
Acute kidney injury	1.92 (1.61–2.28)	<0.001
Mechanical ventilation	21.08 (17.40–25.55)	<0.001
Dialysis	1.78 (1.29–2.45)	<0.001

Survey-weighted logistic regression including all demographic, organ-specific, and complication variables simultaneously (full model). SS cohort only (n = 54,526 unweighted).

Table VI. Racial and Ethnic Disparities in Outcomes Among Hospitalized Sjögren's Syndrome Patients

Race/Ethnicity	Mortality OR (95% CI)	P-value	Adjusted LOS days (diff.)	Adjusted Charges $ (diff.)
White (reference)	1	—	4.8	$55,932
Black	1.24 (1.01–1.51)	0.036	5.59 (+0.80)	$61,922 (+$5,990)
Hispanic	1.34 (1.07–1.67)	0.010	5.14 (+0.34)	$75,613 (+$19,681)
Asian/Pacific Islander	1.67 (1.20–2.31)	0.002	5.40 (+0.60)	$78,575 (+$22,643)
Other	1.30 (0.92–1.82)	0.137	5.15 (+0.35)	$66,077 (+$10,145)

Mortality ORs from survey-weighted logistic regression adjusted for age, sex, insurance, and Elixhauser comorbidity burden. Adjusted LOS and charges from survey-weighted linear regression with predictive margins. Differences in parentheses are relative to White reference group.

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Supplementary Material

Supplementary Table S1. Nested Multivariable Models for In-Hospital Mortality: Sequential Variable Addition

Predictor	Model 1 Demographics	Model 2 + Organs	Model 3 + Complications	Model 4 Full
Demographics				
Age 65–74 (ref: 18–39)	3.28***	3.30***	3.50***	3.46***
Age ≥75	4.25***	4.20***	5.85***	5.43***
Female	0.71***	0.72***	0.81*	0.84*
Asian/PI (ref: White)	1.56**	1.55**	1.65**	1.64**
Self-pay/Other (ref: Medicare)	2.01***	1.99***	1.98***	1.95***
Elixhauser ≥5 (ref: 1–2)	12.64***	11.47***	3.60***	3.61***
Organ Involvement				
ILD	—	2.20***	—	2.10***
PAH	—	1.37***	—	1.41**
Renal involvement	—	0.83	—	0.49***
Hematologic	—	1.71***	—	1.16
Complications				
Sepsis	—	—	2.68***	2.80***
Stroke	—	—	2.61***	2.78***
Any malignancy	—	—	2.38***	2.46***
AKI	—	—	1.83***	1.92***
Mech. ventilation	—	—	21.57***	21.08***
Dialysis	—	—	1.55**	1.78***

*Values are adjusted odds ratios. Model 1: demographics, insurance, comorbidity burden, hospital characteristics. Model 2: Model 1 + organ-specific involvement. Model 3: Model 1 + acute complications and procedures. Model 4: full model. — = variable not included. *P < 0.05; **P < 0.01; ***P < 0.001.*

Supplementary Table S2. Insurance, Hospital, and Regional Disparities in Outcomes Among Hospitalized Sjögren's Syndrome Patients

Factor	Mortality OR (95% CI)	P-value	Adj. LOS (days)	Adj. Charges ($)
Insurance (ref: Medicare)				
Medicare (reference)	1.00	—	5.08	$58,094
Medicaid	1.25 (0.93–1.68)	0.157	5.66 (+0.70)	$61,699
Private	1.41 (1.17–1.70)	<0.001	5.09 (+0.01)	$62,825
Self-pay/Other	2.01 (1.53–2.64)	<0.001	5.15 (+0.07)	$59,404
Hospital teaching status (ref: Rural)				
Rural (reference)	1.00	—	4.58	$35,114
Urban non-teaching	0.98 (0.74–1.29)	0.886	4.70	$57,685
Urban teaching	1.03 (0.80–1.33)	0.314	5.26	$66,748
Hospital region (ref: Northeast)				
Northeast (reference)	1.00	—	5.36	$64,132
Midwest	1.28 (1.04–1.59)	0.022	4.94	$50,937
South	1.21 (0.99–1.47)	0.057	5.22	$60,986
West	0.99 (0.78–1.25)	0.912	4.86	$79,590

All models adjusted for age, sex, race/ethnicity, and Elixhauser comorbidity burden. Mortality ORs from survey-weighted logistic regression. Adjusted LOS and charges from survey-weighted linear regression with predictive margins.

Supplementary Table S3. Comparison of Key Mortality Predictors Across Sensitivity Analyses

	Primary Model	S1: Non-Elective	S3: Primary SS	S5: Excl. 2020
Predictor	(n=54,526)	(n=42,726)	(n=32,642)	(n=43,634)
Mechanical ventilation	21.12 (17.81–25.06)	21.38 (17.95–25.46)	19.71 (15.73–24.71)	20.78 (17.04–25.34)
Sepsis	2.79 (2.30–3.38)	2.64 (2.17–3.21)	3.18 (2.48–4.09)	3.00 (2.39–3.76)
Stroke	2.78 (2.02–3.83)	2.54 (1.84–3.50)	2.64 (1.75–4.00)	2.97 (2.06–4.27)
Malignancy	2.46 (1.98–3.06)	2.60 (2.07–3.25)	2.60 (2.00–3.38)	2.48 (1.93–3.18)
Interstitial lung disease	2.11 (1.73–2.57)	2.03 (1.66–2.49)	2.08 (1.58–2.72)	2.07 (1.66–2.58)
Acute kidney injury	1.92 (1.65–2.23)	1.83 (1.57–2.14)	1.79 (1.47–2.18)	1.84 (1.54–2.19)
Dialysis	1.75 (1.27–2.43)	1.65 (1.18–2.30)	1.97 (1.29–2.99)	2.04 (1.42–2.91)
Acute myocardial infarction	1.60 (1.23–2.07)	1.56 (1.20–2.04)	1.61 (1.14–2.28)	1.37 (1.00–1.87)
Venous thromboembolism	1.59 (1.20–2.10)	1.51 (1.13–2.01)	1.43 (0.99–2.07)	1.64 (1.20–2.25)
Heart failure	1.25 (1.06–1.47)	1.21 (1.02–1.43)	1.25 (1.00–1.54)	1.36 (1.13–1.65)
Pulmonary arterial hypertension	1.41 (1.15–1.73)	1.43 (1.16–1.76)	1.58 (1.21–2.05)	1.43 (1.13–1.81)
Any infection	1.37 (1.14–1.64)	1.30 (1.08–1.57)	1.38 (1.09–1.75)	1.28 (1.03–1.58)
Hematologic involvement	1.16 (0.84–1.62)	1.10 (0.79–1.54)	0.93 (0.60–1.44)	1.25 (0.87–1.81)
Renal involvement	0.50 (0.37–0.69)	0.52 (0.37–0.71)	0.41 (0.27–0.61)	0.43 (0.29–0.63)
Lymphoma	0.70 (0.47–1.04)	0.69 (0.46–1.05)	0.74 (0.46–1.21)	0.73 (0.47–1.14)
Female sex	0.84 (0.68–1.04)	0.86 (0.68–1.08)	0.77 (0.59–0.99)	0.79 (0.62–1.01)
Age ≥75 years	5.43 (3.41–8.66)	4.52 (2.81–7.29)	5.06 (2.40–10.65)	6.56 (3.83–11.23)
Elixhauser ≥5	3.60 (2.26–5.75)	3.11 (1.90–5.08)	3.53 (1.93–6.45)	4.41 (2.50–7.78)

Values are adjusted odds ratios (95% confidence intervals) from survey-weighted logistic regression using the full Model 4 specification: demographics (age, sex), race/ethnicity, insurance, Elixhauser comorbidity categories, hospital characteristics (teaching status, bed size, region), organ-specific involvement (ILD, PAH, renal, CNS, PNS, hematologic), infections, sepsis, lymphoma, malignancy, cardiovascular events (AMI, stroke, VTE, heart failure, valvular disease), AKI, mechanical ventilation, and dialysis.
S1: restricted to non-elective admissions. S3: approximate primary Sjögren's syndrome, excluding hospitalizations with concurrent rheumatoid arthritis (M05, M06), systemic lupus erythematosus (M32), systemic sclerosis (M34), dermatomyositis/polymyositis (M33), or mixed connective tissue disease (M35.1). S5: excluding 2020 hospitalizations. S2 (principal diagnosis only; n≈162) and S4 (age-stratified) are reported in the Results text only.