

Association of Acute Pain and Fatigue on Health Care Resource Utilization and Costs in Patients With Sickle Cell Disease in the United States

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Plain language summary

Why does it matter? Sickle cell disease (SCD) is a lifelong condition that affects red blood cells and commonly causes pain and fatigue (which may include symptoms such as tiredness, exhaustion, and lack of energy). It is not clear how much these symptoms affect health care costs.

How does it work? This study used claims and electronic health record data with personal information removed to examine whether acute pain and fatigue in patients with SCD are associated with increased health care use and costs in the United States.

What did we find? Patients with SCD who experienced acute pain and fatigue had higher health care use and total costs. This highlights the need for treatments that better address pain and tiredness in patients with SCD.

Introduction

- Sickle cell disease (SCD), a chronic debilitating disease caused by abnormalities in hemoglobin, affects approximately 100,000 individuals in the United States¹
- Patients with SCD report experiencing pain on >50% of all days²
- Daily fatigue is reported in >80% of patients with SCD³
- The economic burden associated with these symptoms remains unclear
- Understanding how acute pain and fatigue are associated with health care resource utilization (HCRU) and medical costs may provide insights into the potential cost offsets and value of SCD therapies
- This study evaluated whether acute pain and fatigue in patients with SCD are associated with increased HCRU and costs in the United States

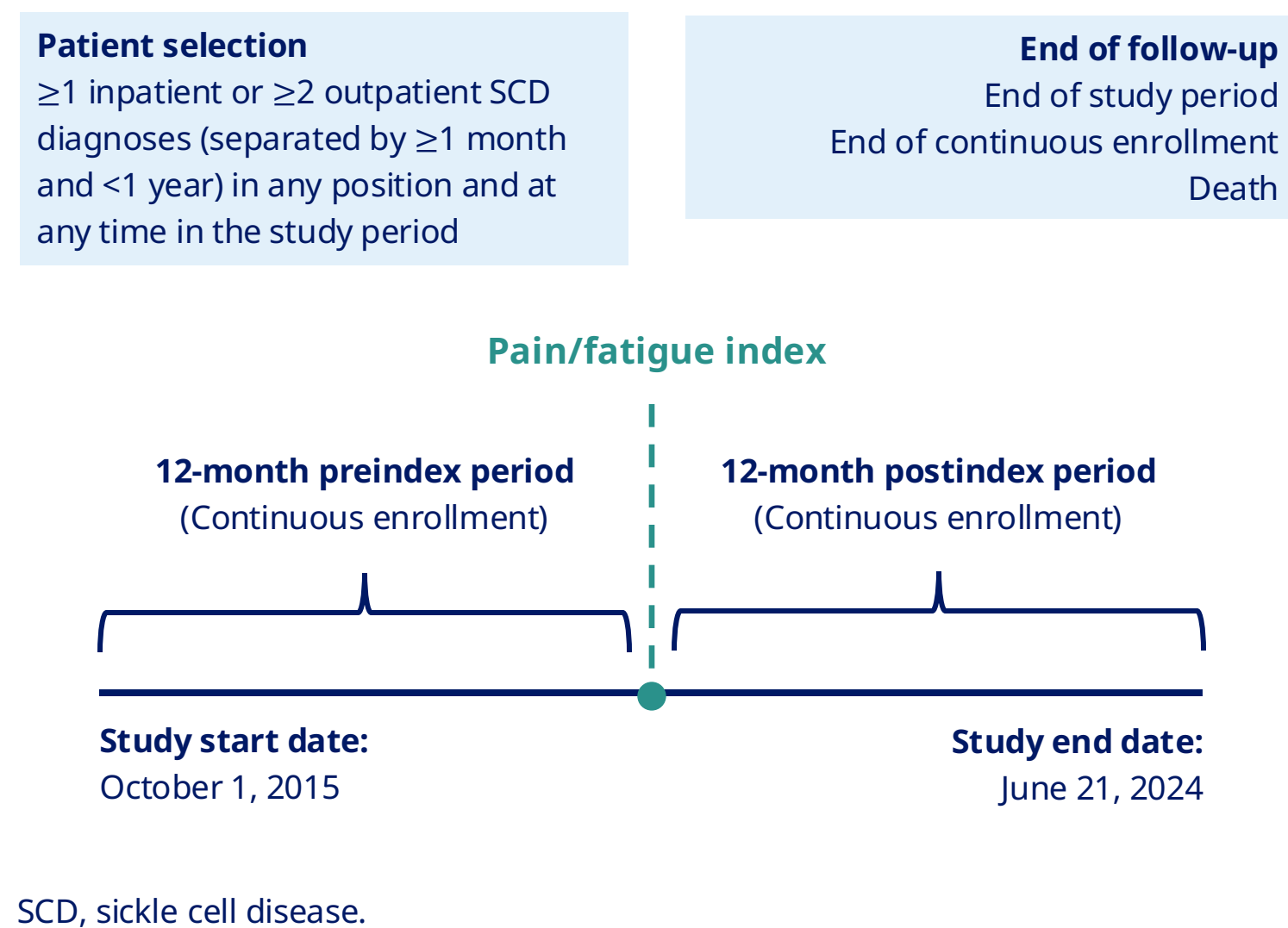
Methods

- This retrospective, longitudinal cohort study used data from the TriNetX Linked Network claims database and TriNetX Dataworks-USA electronic health record data
- Patients were aged ≥12 years and were diagnosed with SCD between October 1, 2015, and June 21, 2024
- Patients with sickle cell trait and evidence of gene therapy or stem cell transplantation were excluded
- Clinical characteristics and treatments were assessed during a 12-month baseline period (**Figure 1**)
- Cases were required to meet definitions of acute pain and fatigue within a 12-month period
 - Acute pain was defined as an emergency department (ED) or inpatient encounter documented with an *International Classification of Diseases, Tenth Revision, Clinical Modification* code for generic pain or SCD crisis, where either intravenous pain medication was administered during the encounter⁴ or an opioid prescription was given within 7 days of the respective ED/inpatient encounter

Methods (cont'd)

- Fatigue was defined as hemoglobin levels ≤10.0 g/dL (a proxy for fatigue, based on National Cancer Institute gradings of anemia⁵) or a diagnosis using *ICD-10-CM* codes for fatigue
- The control group consisted of patients who did not report pain or fatigue during the study period
- The percentage of patients with inpatient, outpatient, ED, and pharmacy care and the mean cost over a 1-year postindex period were compared between cases and controls
- Logistic regression models were used to estimate adjusted odds ratios for HCRU. Linear regression models were used to estimate incremental total cost (2023 US dollars). All models adjusted for SCD genotype, baseline treatments, and clinical and demographic characteristics, with pain and fatigue as a main effect

Figure 1: Study design



Results

- This study included 1,075 cases and 451 controls
- Baseline demographics and clinical characteristics can be found in **Table 1**

Table 1: Baseline demographics and clinical characteristics

	With pain and fatigue (n=1,075)	Without pain or fatigue (n=451)	P value
Age, y			.045
Mean (SD)	33.9 (12.3)	33.9 (16.8)	
Sex, n (%)			.023
Female	623 (58.0)	232 (51.4)	
Male	452 (42.0)	219 (48.6)	
Comorbidities, n (%)^a			
Chronic pulmonary disease	401 (37.3)	68 (15.1)	<.001
Hypertension	369 (34.3)	79 (17.5)	<.001
Pneumonia	331 (30.8)	17 (3.8)	<.001
Asthma	324 (30.1)	61 (13.5)	<.001
Anxiety	299 (27.8)	58 (12.9)	<.001
Urinary tract infection	224 (20.8)	28 (6.2)	<.001
Treatments, n (%)^b			
Pain medications	972 (90.4)	195 (43.2)	<.001
Hydroxyurea	428 (39.8)	42 (9.3)	<.001
Transfusion, n (%)			<.001
	496 (46.1)	49 (10.9)	

SCD, sickle cell disease.

^aShown are those comorbidities occurring in ≥20% of either group. Additional SCD-related comorbidities occurring in <20% of both groups include acute cholecystitis/cholangitis, acute myocardial infarction, chronic obstructive pulmonary disease, depression, diabetes mellitus, gout, heart failure, hyperlipidemia, obesity, osteoporosis, sepsis, spinal cord injury, and venous thromboembolism. ^bShown are those treatments received by ≥20% of either group. Additional treatments received by <20% of both groups include erythropoietin-stimulating agents, crizanlizumab-tmca, L-glutamine, and voxelotor.

P values are based on nonparametric Wilcoxon tests for continuous variables and chi-square or Fisher exact tests of independence for categorical variables.

- Compared with controls, patients with pain and fatigue were more likely to be female ($P<.05$) and to have received hydroxyurea treatment, pain medications, and transfusions at baseline (all $P<.001$; **Table 1**)
- Patients with pain and fatigue experienced significantly more comorbidities, including chronic pulmonary disease, hypertension, pneumonia, and asthma (all $P<.001$; **Table 1**)
- Twelve-month inpatient, outpatient, ED, and pharmacy utilization were all much greater among patients with pain and fatigue than among controls (**Figures 2 and 3**)
- Strong effect sizes were observed for all covariates, with odds ratios ranging from 2.37 (95% CI, 1.31-4.29) for outpatient care to 10.86 (95% CI, 7.46-15.81) for inpatient care (all $P<.001$)
- Adjusted all-cause costs were \$7,689 higher per patient per year in patients with pain and fatigue vs controls (95% CI, \$1,853-\$13,524; $P<.01$)

Figure 2: 12-month unadjusted HCRU

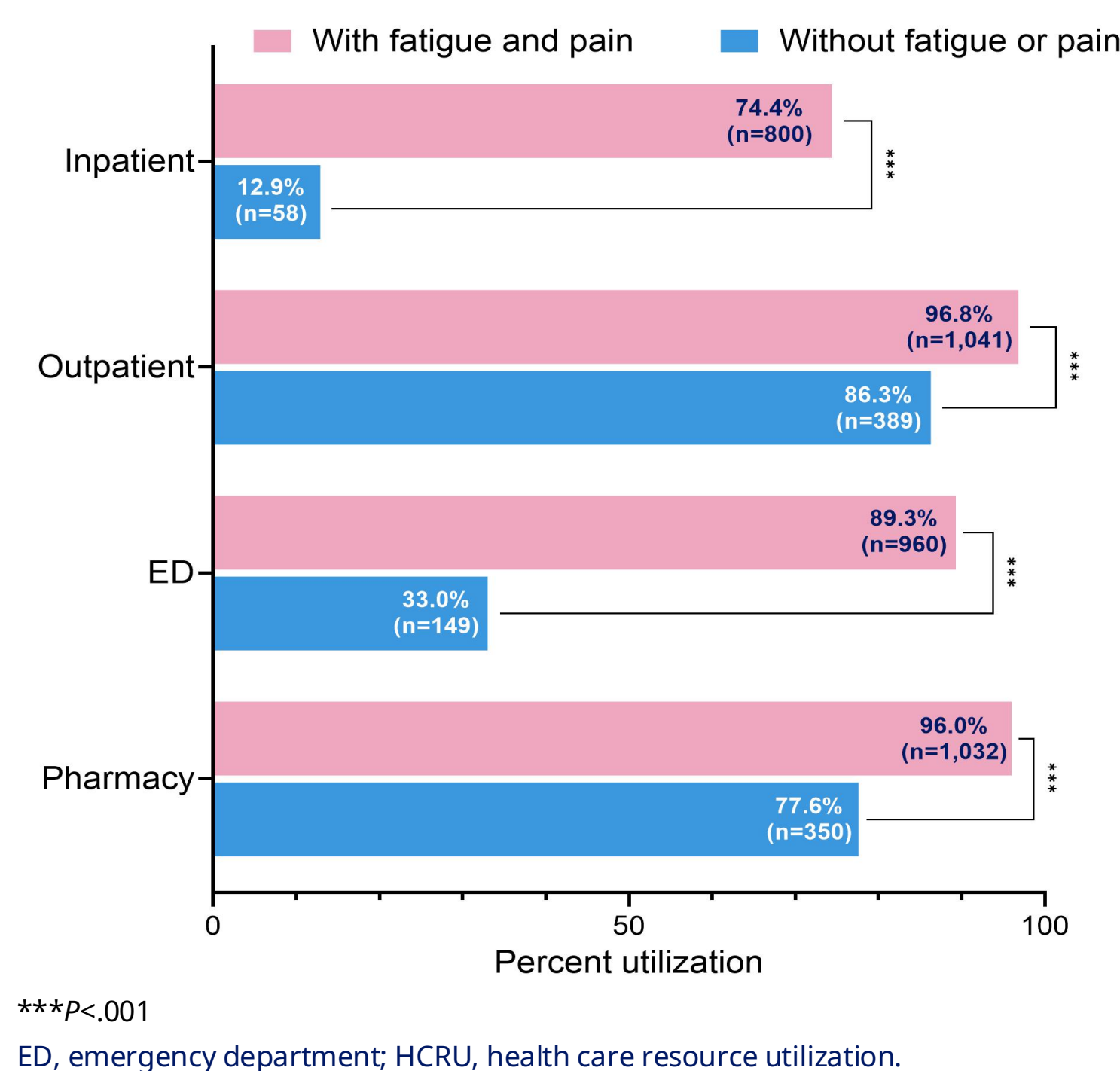
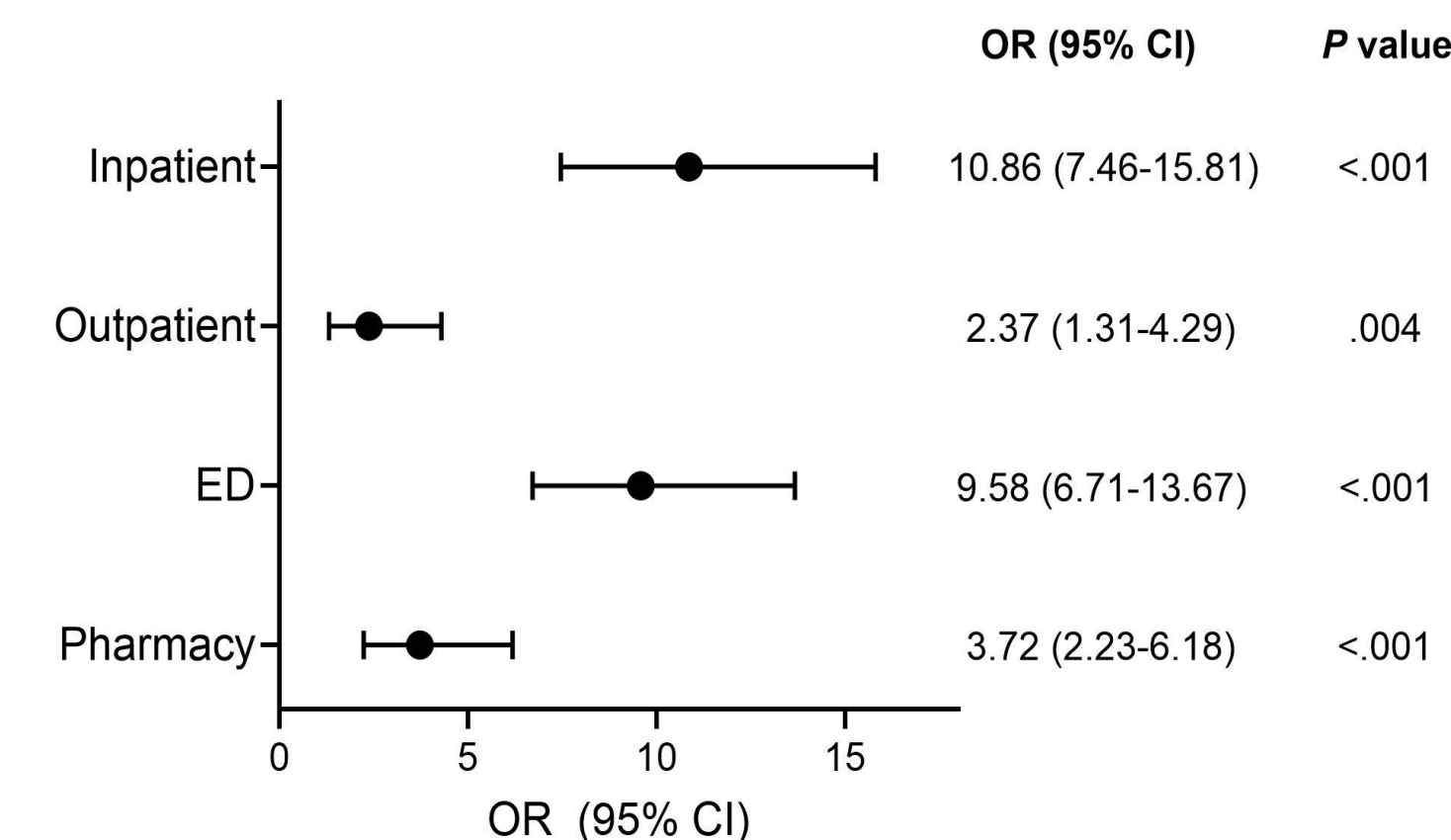


Figure 3: 12-month regression-adjusted HCRU (acute pain and fatigue vs controls)



Key Result: Inpatient, outpatient, ED, and pharmacy utilization were all significantly higher (all $P<.001$) in patients with **pain and fatigue**, resulting in adjusted all-cause costs that were **\$7,689 higher** per patient per year than those of controls

Conclusions

- Pain and fatigue are associated with higher costs and HCRU among patients with SCD, highlighting the **substantial and previously underrecognized** economic burden of these symptoms among patients with SCD
- These findings reinforce the need for treatments that address unmet needs for the **management of acute pain and fatigue** among patients with SCD

Jigar R. Rajpura, Jing Voon Chen, and Adam Wufsus are employees of Novo Nordisk Inc. Mihail Samnaliev, Yi Pan, Matthew Sussman, and Scott Bunner report no conflicts of interest to disclose.

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