Journal of Health Economics and Outcomes Research

Online Supplementary Material

Impact of Acute Pain and Fatigue on Healthcare Resource Utilization and Costs in Sickle Cell Disease in the United States. *JHEOR*. 2026;13(2):259-270. doi:10.36469/jheor.2026.171490

Figure S1: Study Design 1

Figure S2: Patient Flow for the Evaluation of Acute Pain and Fatigue 2

Figure S3: Patient Flow for the Evaluation of Acute Pain 3

Figure S4: Patient Flow for the Evaluation of Fatigue 4

Figure S5: 12-Month Unadjusted HCRU and Average Costs Specific to Acute Pain and Fatigue 5

Figure S6: 12-Month Unadjusted HCRU and Average Costs Specific to Acute Pain 6

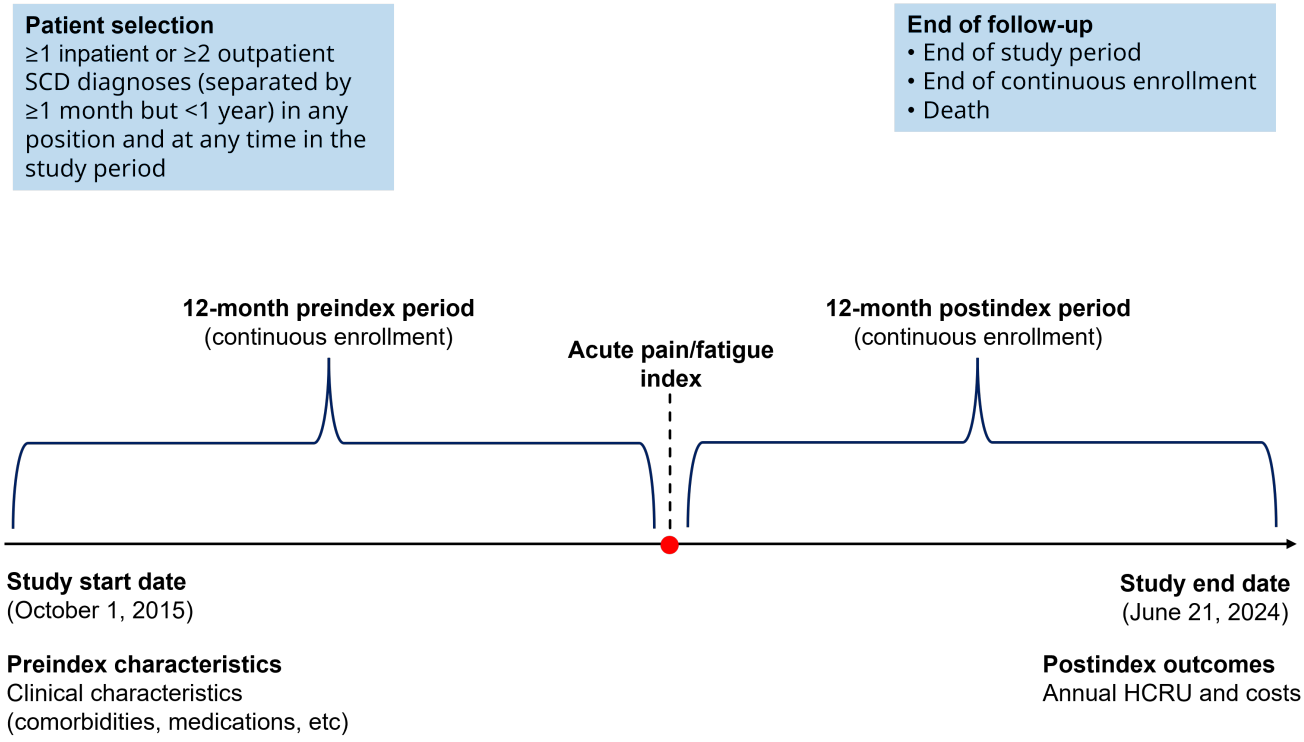
Figure S7: 12-Month Unadjusted HCRU and Average Costs Specific to Fatigue 7

Table S1: Sensitivity Analyses, HCRU, and Costs Associated with Fatigue Diagnosis 8

This supplementary material has been provided by the authors to give readers additional information about their work.

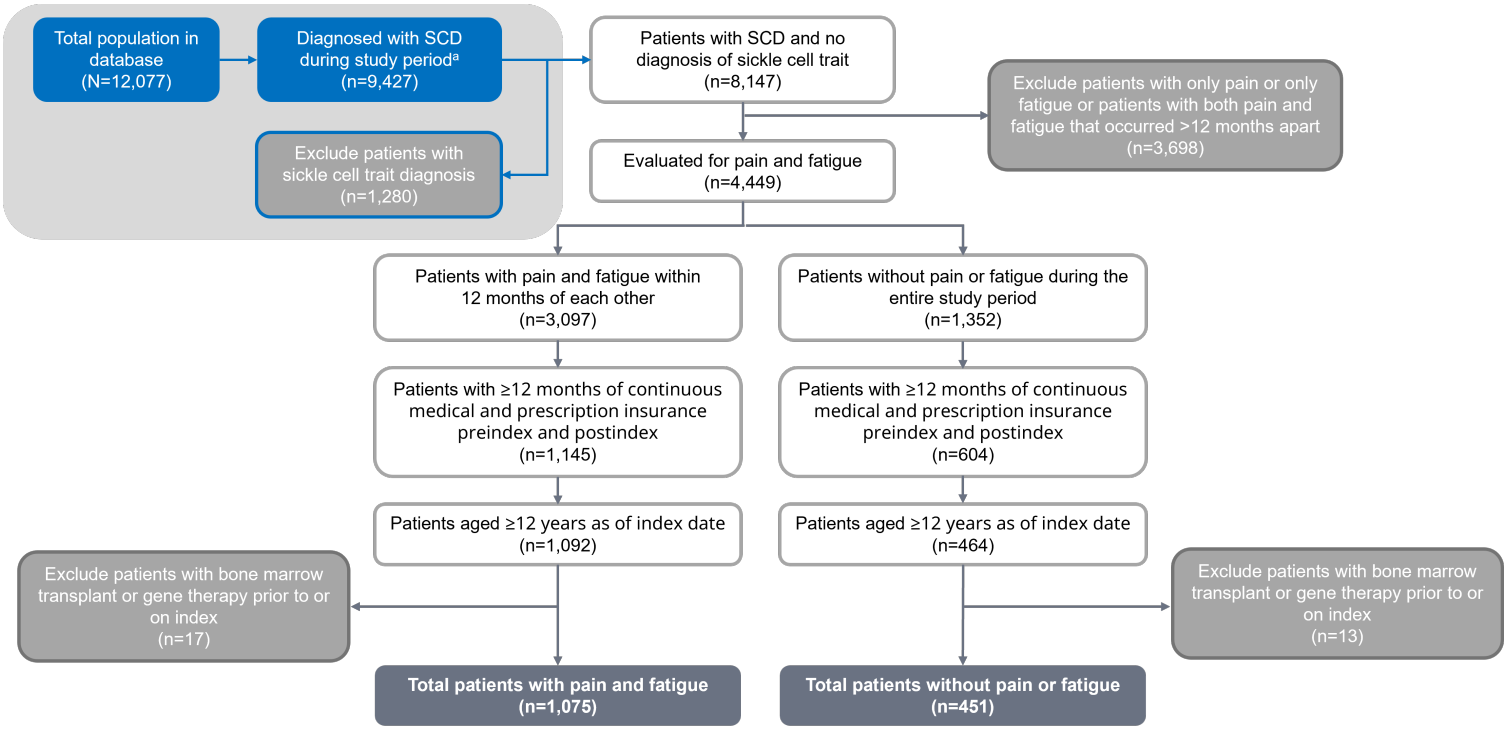
This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CCBY-4.0). View this license's legal deed at http://creativecommons.org/licenses/by/4.0 and legal code at http://creativecommons.org/licenses/by/4.0/legalcode for more information.

Figure S1. Study Design



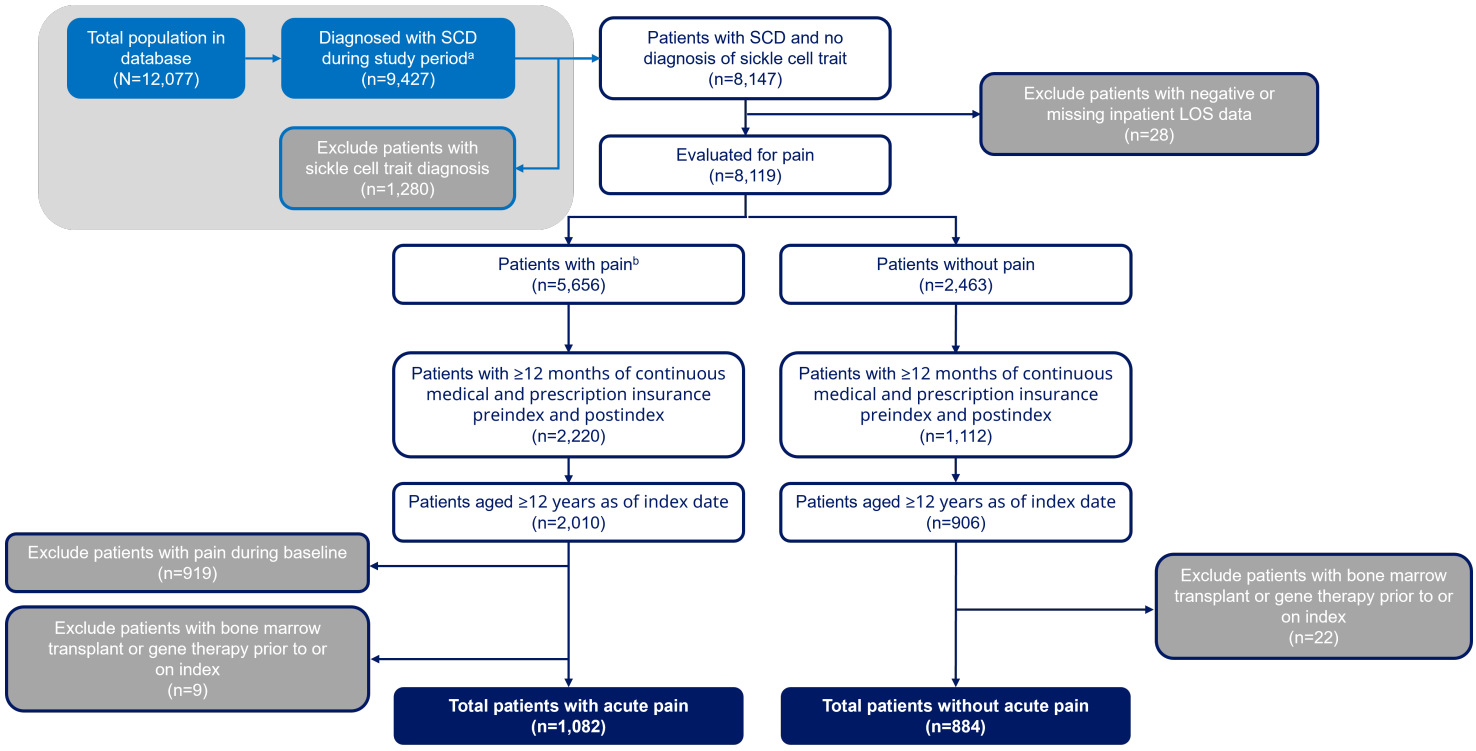
Abbreviations: HCRU, healthcare resource utilization; SCD, sickle cell disease.

Figure S2. Patient Flow for the Evaluation of Acute Pain and Fatigue



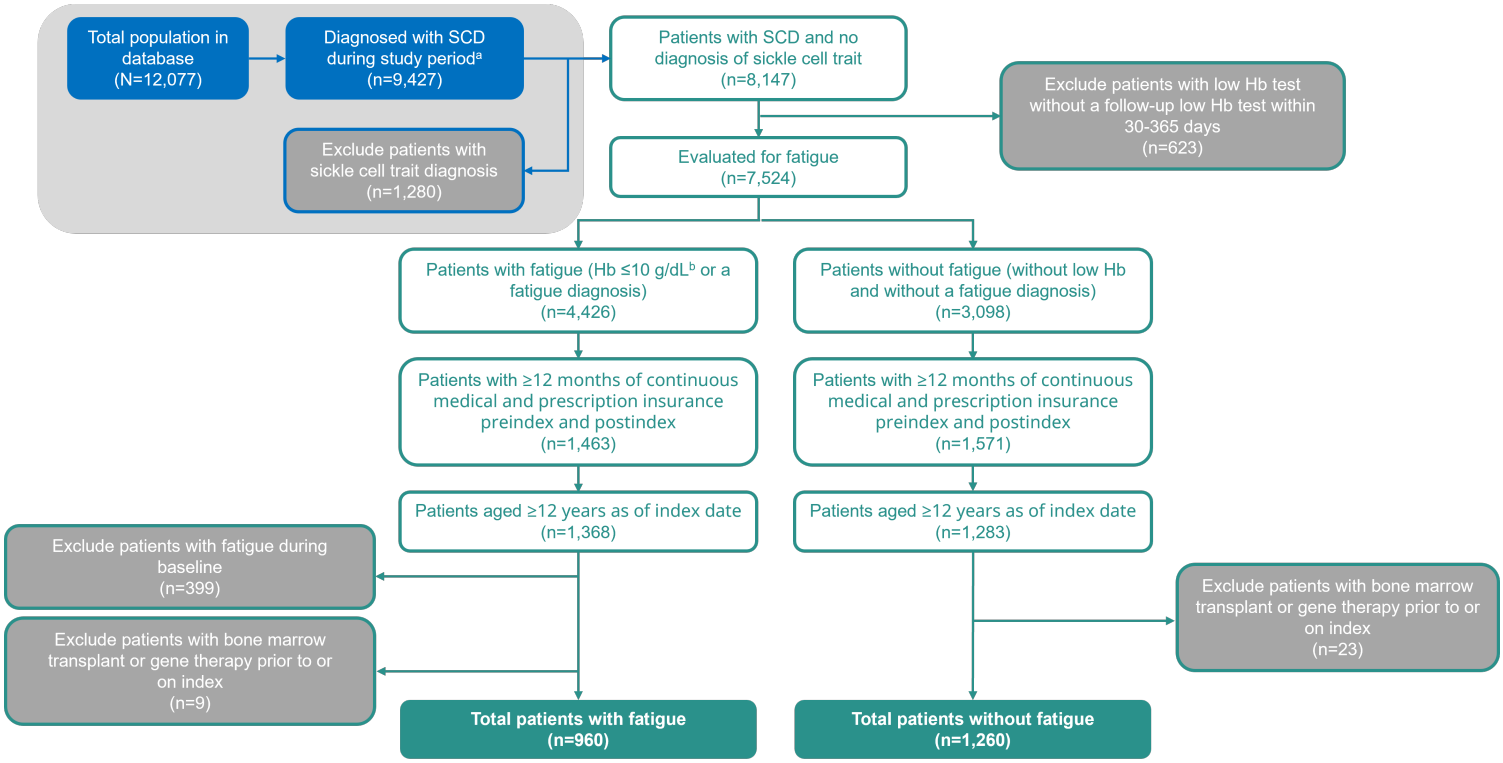
Abbreviations: *ICD-10-CM*, *International Classification of Diseases, Tenth Revision, Clinical Modification*; SCD, sickle cell disease.
[a]At least 1 SCD *ICD-10-CM* diagnosis code (including D57, D57.* [except for D57.3; sickle cell trait], D57.*) in any position in the inpatient setting, or 2 separate SCD diagnoses in the outpatient setting occurring at least 1 month apart but less than 1 year apart during the study period.

Figure S3. Patient Flow for the Evaluation of Acute Pain



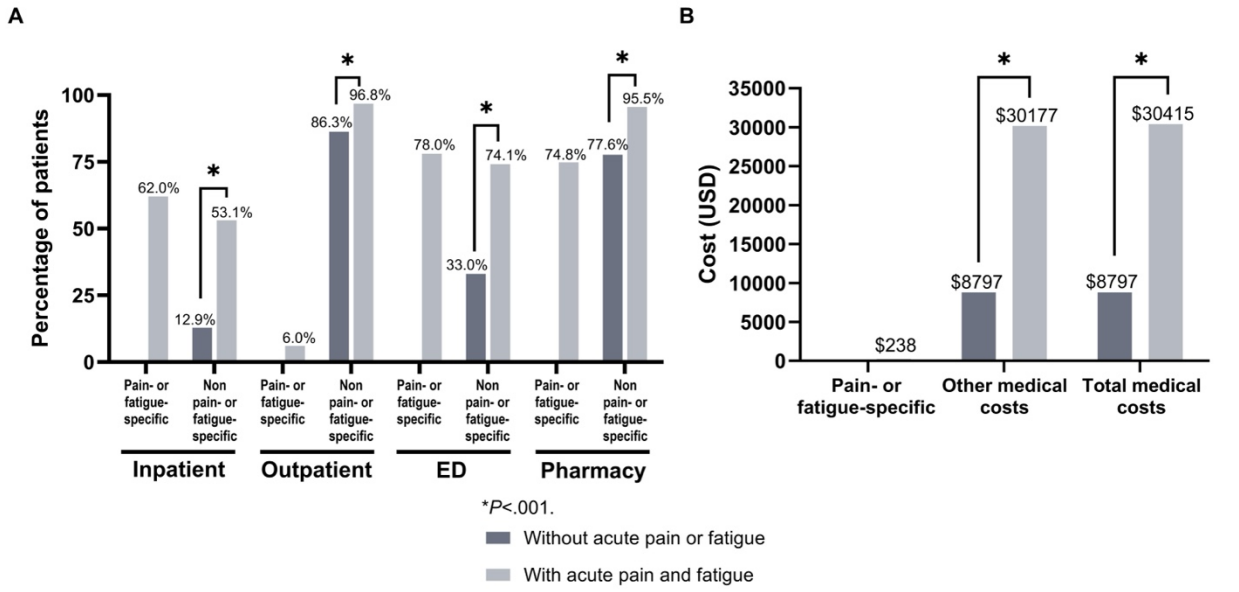
Abbreviations: ED, emergency department; *ICD-10-CM*, *International Classification of Diseases, Tenth Revision, Clinical Modification*; IV, intravenous; LOS, length of stay; SCD, sickle cell disease.
[a]At least 1 SCD *ICD-10-CM* diagnosis code (including D57, D57.* [except for D57.3; sickle cell trait], D57.*) in any position in the inpatient setting, or 2 separate SCD diagnoses in the outpatient setting occurring at least 1 month apart but less than 1 year apart during the study period. [b]The acute pain cohort was based on the algorithm described by Singh et al, in which a pain crisis was defined using the following criteria: (1) ED or inpatient encounter, (2) with an *ICD-10-CM* code for generic pain or SCD crisis, where (3) IV pain medication was administered.[10] The Singh algorithm was complemented with opioids for the treatment of pain during the inpatient/ED visit or within 7 days after discharge/ED visit.

Figure S4. Patient Flow for the Evaluation of Fatigue



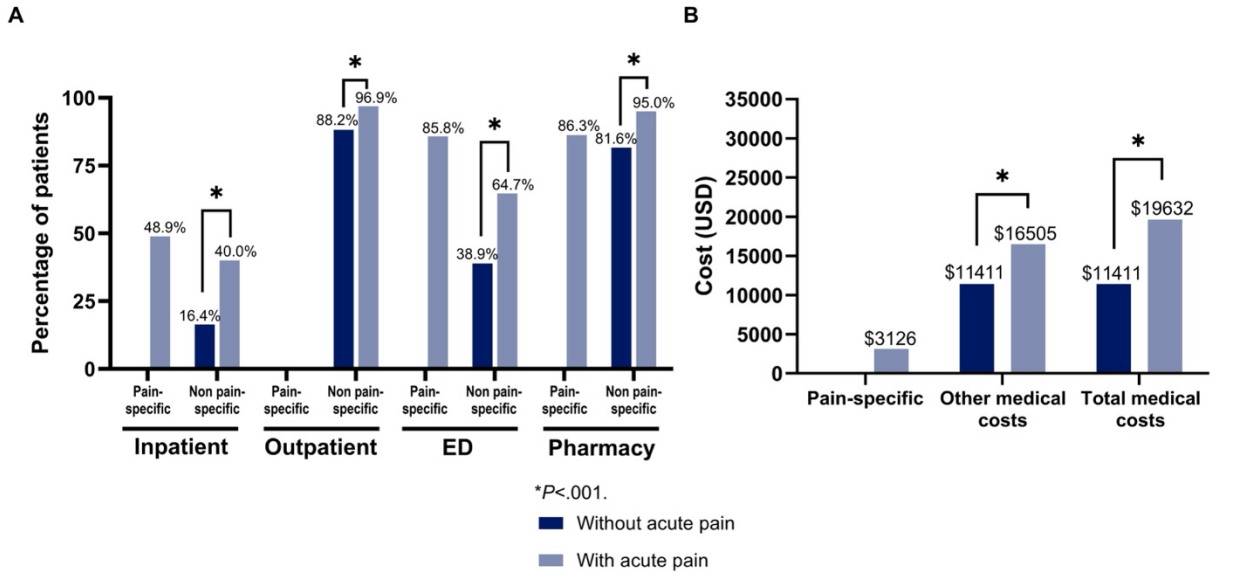
Abbreviations: Hb, hemoglobin; *ICD-10-CM*, *International Classification of Diseases, Tenth Revision, Clinical Modification*; SCD, sickle cell disease.
[a]At least 1 SCD *ICD-10-CM* diagnosis code (including D57, D57.* [except for D57.3; sickle cell trait], D57.*) in any position in the inpatient setting, or 2 separate SCD diagnoses in the outpatient setting occurring at least 1 month apart but less than 1 year apart during the study period. [b]Requiring a low Hb (≤10 g/dL) test result and a prior Hb test performed within 30-365 days before the low Hb test.

Figure S5. 12-Month Unadjusted HCRU and Average Costs[a] Specific to Acute Pain and Fatigue



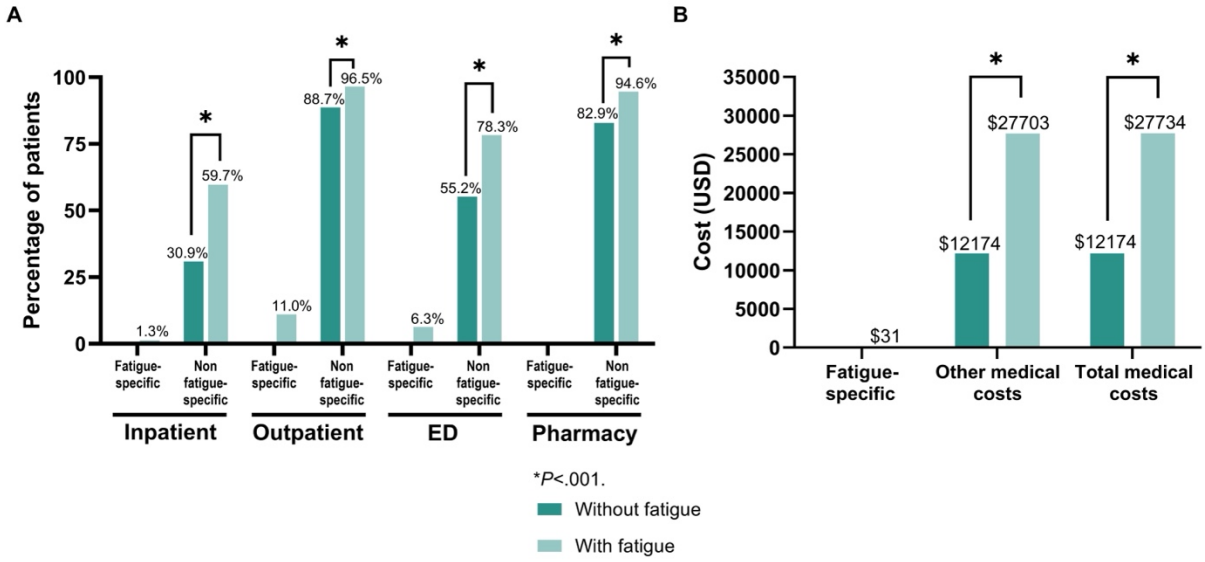
Abbreviations: ED, emergency department; HCRU, healthcare resource utilization.
[a]Acute pain-specific HCRU and costs were defined as inpatient/ED utilization encounters and costs (including opioid prescriptions within 7 days after the respective inpatient/ED encounter) that were used for the acute pain cohort assignment. Fatigue-specific utilization and costs were based on utilization with a primary diagnosis of fatigue (medications were not used in the definition of fatigue-specific utilization and costs). Because of these definitions, the without acute pain or fatigue cohort has zero values for inpatient, outpatient, ED, pharmacy utilization, and acute pain- or fatigue-specific costs.

Figure S6. 12-Month Unadjusted HCRU and Average Costs[a] Specific to Acute Pain



Abbreviations: ED, emergency department; HCRU, healthcare resource utilization.
[a]Acute pain-specific HCRU and costs were based on inpatient/ED utilization encounters and costs (including opioid prescriptions within 7 days after the respective inpatient/ED visit) that were used for the acute pain cohort assignment. Because of that definition, the without acute pain cohort has zero values for inpatient, ED, pharmacy utilization, and acute pain-specific costs, and both cohorts have zero values for outpatient utilization.

Figure S7. 12-Month Unadjusted HCRU and Average Costs[a] Specific to Fatigue



Abbreviations: ED, emergency department; HCRU, healthcare resource utilization.
[a]Fatigue-specific utilization and costs were based on utilization with a primary diagnosis of fatigue (medications were not used in the definition of fatigue-specific utilization and costs). Because of that definition, the without fatigue cohort has zero values for inpatient, outpatient, ED utilization, and fatigue-specific costs, and both cohorts have zero values for pharmacy utilization.

Table S1. Sensitivity Analyses, HCRU, and Costs Associated with Fatigue Diagnosis[a]

	Odds Ratio	**95% CI**	***P* Value**
Inpatient	1.90	1.52; 2.38	<.001
Outpatient	9.19	3.65; 23.19	<.001
ED	2.62	2.02; 3.40	<.001
Prescriptions	5.81	3.27; 10.33	<.001
	Incremental		
Total inflation-adjusted costs	$8166	$4267; $12 065	<.001

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; ED, emergency department; HCRU, healthcare resource utilization; SCD, sickle cell disease.

[a]Adjusting at baseline for sex, age, race, ethnicity, type of insurance, CCI score, SCD genotype, SCD-related comorbidities, SCD-specific treatments, transfusions, and anxiety or depression.