Economic Burden of Managing Vaso-Occlusive Crisis among Patients with Sickle Cell Disease in the United States: A Systematic Review

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BACKGROUND

- Vaso-occlusive crises (VOCs) are the hallmark complication of sickle cell disease (SCD), characterized by sudden, severe pain that often requires emergency medical attention.[7]
- These episodes are driven by inflammation and endothelial dysfunction, leading to vascular injury.[6,7]
- VOCs significantly impair quality of life and are the primary cause of hospitalization among individuals with SCD in the United States.[2,4]
- The frequency and intensity of VOCs contribute to substantial healthcare resource utilization and long-term clinical burden.[2]
- Assessing the **economic impact of VOCs** is vital to inform healthcare policy, prioritize resource allocation, and advocate for more effective interventions.

OBJECTIVES

- To synthesize existing literature on the direct economic burden of managing Vaso-occlusive crises (VOCs) among patients with sickle cell disease (SCD) in the United States.

METHODS

Study Design

This study adopted a standard systematic review procedure.

Protocol and Registration

The review protocol was developed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and registered with an International Prospective Register of Systematic Reviews (PROSPERO) with ID; CRD42024586629

INCLUSION CRITERIA

- Medical costs specific to VOC among patients with SCD
- Original Article
- Conducted in the United States

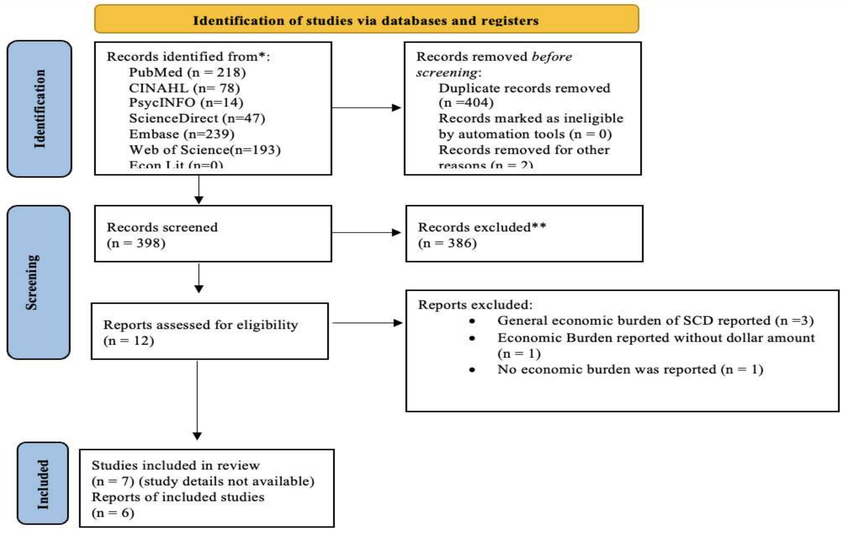
EXCLUSION CRITERIA

- Not a literature review or systematic review
- Should not be conducted outside United States
- Not a general economic burden in patients with SCD

Data Sources and Search Strategy

- Seven electronic databases were searched: PubMed, CINAHL, Web of Science, PsycINFO, EconLit, ScienceDirect, and Embase.
- Search terms included combinations of: “sickle cell disease,” “Vaso-occlusive crisis,” “healthcare cost,” “economic burden,” and “United States.”
- The search covered articles published from 2008 to 2024.
- Reported costs were adjusted to 2024 U.S. dollars using the Consumer Price Index (CPI) to allow for comparison across studies.

PRISMA 2020 flow diagram for new systematic reviews



RESULTS

Author	Year	Database	Study period	Patient age	Study Design	VOC Amount($)	Cost Item	Year of cost	Adjusted Total Cost(2024 Inflation rate)
Candrilli, S.D. et al [1]	2011	North Carolina Medicaid program	2000-2008	< 65 years	Restrospective	Non-Hydroxyurea adherent group = $8,887.Hydroxyurea adherent group $3,094	Vaso -occlusive event related cost	2008	Non-Hydroxyurea adherent group ; $13,022.51, Hydroxyurea adherent group ;$4,533.77
Shah, N.R. et al [2]	2020	IBM Truven Health MarketScan Commercial (MarketScan),Research Identifiable File (RIF) Medicaid Analytic eXtract (MAX),RIF Medicare encounter final files with drug event linkage Analytic eXtract (MAX)	Marketscan(2000-2018),Medicaid(2008-2014), Medicare(2012-2016)	≥16 years	Retrospective	**IP Costs** - Commercial: $20,839.00, Medicaid: $24,179.00, Medicare: $22,622.00; **OP Costs** - Commercial: $9,614.00, Medicaid: $4,260.00, Medicare: $8,553.00; **ER Costs** - Commercial: $2,693.00, Medicaid: $1,878.00, Medicare: $2,901.00	Medical services with a VOC-related diagnosis recorded within 7 days following an initial VOC-related diagnosis in an emergency room (ER) or outpatient (OP) setting.Inpatient (IP) readmission recorded within 14 days of a previous IP stay	2018	**IP Costs** - Commercial: $26,182.30, Medicaid: $30,378.70, Medicare: $28,422.48; **OP Costs** - Commercial: $12,079.11, Medicaid: $5,352.30, Medicare: $10,746.06; **ER Costs** - Commercial: $3,383.51, Medicaid: $2,359.54, Medicare: $3,644.84
Bou-Maroun, L.M. et al [3]	2018	Kids Inpatient Database (KID)	2009-2012	<21years	Retrrospective	$588,632,958	Hospitalization for VOC crisis(annual)	2012	$808,860,762.12
Shah, N.. et al [4]	2020	United States Medicaid MAX	2009-2012	≥18years	Retrospective	**Inpatient VOCs** = US$11,398. **ER** =US$1,072. **Outpatient** = $695. Office Settings = US$306	Mean costs per VOC episode	2013	Inpatient VOCs = US$15,436.28. ER =US$1,451.81. Outpatient = $941.24. Office Settings = US$414.41
Raphael, J.L. et al5	2012	Kids Inpatient Database (KID)	2006	≤18years	Retrospective	$10,691	Median total hospital charge for study sample	2006	$16,730.83
Sanni, A. et al [6]	2024	National Inpatient Sample (NIS)	2016-2019	≥18years	Retrospective	Without Opioid use Disorder = $8,020. With Opioid Use Disorder = $9,076	Mean Cost for VOC Hospitalization. Without OUD ,Length of Stay = 5.01 days. With OUD ,LOS =6.16 days	2019	Without Opioid use Disorder = $9,897.06. With Opioid Use Disorder = $11,200.22

FINDINGS

- Six U.S. retrospective studies reported direct VOC costs using databases like MarketScan, Medicaid, and the Kids Inpatient Database.
- Inpatient costs were the highest across all care settings, contributing to an annual hospitalization cost of $808.86 million (adjusted to 2024 rates).
- One of the studies reported a comprehensive cost of VOC across different health setting (office visit, ER, OP and IP with a total of US$13,471
- Median hospital charges per VOC ranged from $16,730.83 to $21,389.78.
- Medicaid inpatient costs were 16.0% higher than commercial insurance and 6.9% higher than Medicare.
- VOC costs were 13.2% higher for patients with opioid use disorders and 65.2% higher for those non-adherent to hydroxyurea therapy.

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CONCLUSIONS

Managing VOCs in SCD patients imposes a substantial economic burden, with costs varying based on the type of medical service, presence of comorbid conditions, and level of treatment adherence.

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