

# **Economic and Clinical Burden of Managing Sickle Cell Disease with Recurrent Vaso-Occlusive Crises in the United States**

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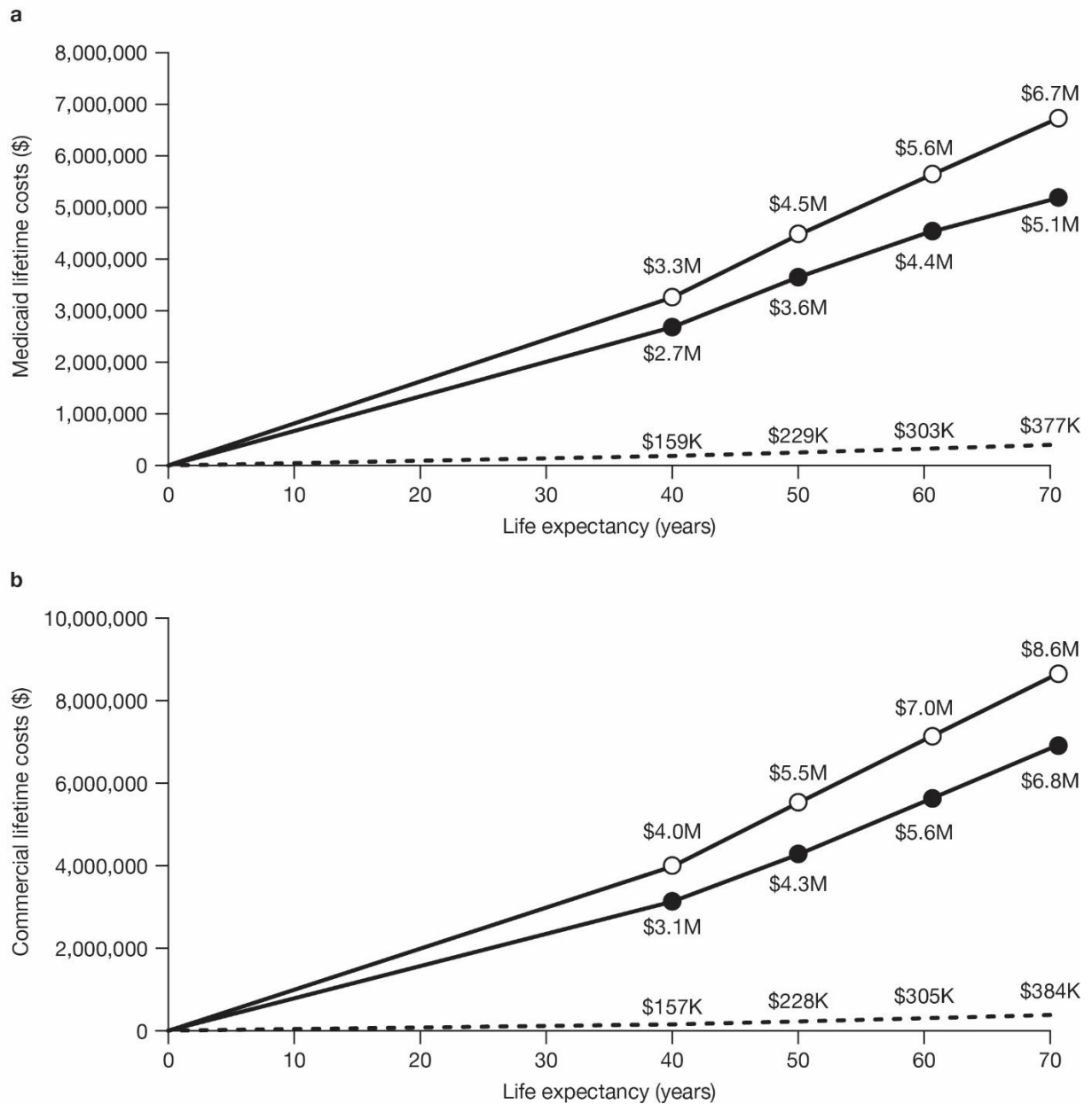
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○ Subgroup of patients with  $\geq 2$  VOCs/year ● Patients with SCD with recurrent VOCs --- Matched controls



**Supplementary Fig. 1** Lifetime healthcare costs for patients with SCD with recurrent VOCs, the subgroup of patients who continued to experience  $\geq 2$  VOCs per year during the variable-length follow-up, and matched controls based on coverage with **a** Medicaid or **b** commercial insurance.

*K* thousand, *M* million, *SCD* sickle cell disease, *VOC* vaso-occlusive crisis

**SUPPLEMENTARY MATERIAL**

**Supplementary Table 1** Clinical complications in patients with SCD with recurrent VOCs by age and number of VOCs<sup>a</sup>

Clinical complication, <i>n</i> (%) <sup>b</sup>	Age (years)			Number of VOCs	
	0 to 11 ( <i>n</i> = 1065)	12 to 35 ( <i>n</i> = 1963)	≥36 ( <i>n</i> = 392)	<2 VOCs per year during follow-up ( <i>n</i> = 1110)	≥2 VOCs per year during follow-up ( <i>n</i> = 2310)
Acute infections	896 (84.1)	1512 (77.0)	288 (73.5)	767 (69.1)	1929 (83.5)
Chronic lung disease	646 (60.7)	866 (44.1)	141 (36.0)	503 (45.3)	1150 (49.8)
Asthma	636 (59.7)	810 (41.3)	107 (27.3)	482 (43.4)	1071 (46.4)
Mental health complications	229 (21.5)	901 (45.9)	177 (45.2)	237 (21.4)	1070 (46.3)
Anxiety	167 (15.7)	592 (30.2)	113 (28.8)	145 (13.1)	727 (31.5)
Depression	122 (11.5)	703 (35.8)	135 (34.4)	168 (15.1)	792 (34.3)
Cardiovascular complications	271 (25.4)	734 (37.4)	227 (57.9)	260 (23.4)	972 (42.1)
Cardiomegaly	244 (22.9)	559 (28.5)	144 (36.7)	186 (16.8)	761 (32.9)
Heart failure	18 (1.7)	206 (10.5)	131 (33.4)	53 (4.8)	302 (13.1)
Pulmonary hypertension	29 (2.7)	277 (14.1)	111 (28.3)	69 (6.2)	348 (15.1)
Bone and joint problems <sup>c</sup>	130 (12.2)	648 (33.0)	168 (42.9)	165 (14.9)	781 (33.8)
Avascular necrosis/osteonecrosis	130 (12.2)	637 (32.5)	153 (39.0)	158 (14.2)	762 (33.0)
Chronic pain	54 (5.1)	700 (35.7)	154 (39.3)	103 (9.3)	805 (34.8)
Iron overload	97 (9.1)	432 (22.0)	106 (27.0)	111 (10.0)	524 (22.7)

Hypercoagulable state	27 (2.5)	418 (21.3)	136 (34.7)	74 (6.7)	507 (21.9)
Gallbladder disease <sup>d</sup>	188 (17.7)	344 (17.5)	41 (10.5)	122 (11.0)	451 (19.5)
Gallstones	176 (16.5)	319 (16.3)	36 (9.2)	114 (10.3)	417 (18.1)

*SCD* sickle cell disease; *VOC* vaso-occlusive crisis

<sup>a</sup>Data were assessed during the variable-length follow-up, beginning on the index date and ending on the earliest date of either inpatient death, end of continuous enrollment, or end of the study period (March 1, 2020)

<sup>b</sup>Clinical complications that occurred in >10% of the patient population are presented

<sup>c</sup>Bone/joint complications included avascular necrosis/osteonecrosis and osteoporosis

<sup>d</sup>Gallbladder disease included chronic cholecystitis, gallstones, and other chronic gallbladder disease

**Supplementary Table 2** Treatment patterns in patients with SCD with recurrent VOCs based on number of VOCs<sup>a</sup>

	<b>&lt;2 VOCs per year during follow-up (<i>n</i> = 1110)</b>	<b>≥2 VOCs per year during follow-up (<i>n</i> = 2310)</b>
Treatment claims, <i>n</i> (%) <sup>b</sup>		
Pain medications	1072 (96.6)	2294 (99.3)
Opioids <sup>c</sup>	973 (87.7)	2227 (96.4)
NSAIDs	927 (83.5)	2122 (91.9)
Gabapentin	98 (8.8)	524 (22.7)
Folic acid	741 (66.8)	1691 (73.2)
Hydroxyurea	647 (58.3)	1678 (72.6)
Penicillin	319 (28.7)	605 (26.2)
Iron chelation therapy	86 (7.7)	382 (16.5)
Treatment claims PPPY, mean (SD) <sup>b</sup>		
Pain medications	6.0 (8.0)	16.4 (15.8)
Opioids <sup>c</sup>	4.0 (7.0)	12.5 (14.1)
NSAIDs	1.8 (2.0)	3.6 (3.9)
Gabapentin	0.2 (1.3)	0.4 (1.3)
Folic acid	2.8 (3.4)	2.5 (3.0)
Hydroxyurea	2.8 (3.6)	2.6 (3.0)
Penicillin	1.6 (4.4)	0.9 (3.2)

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Iron chelation therapy	0.4 (2.2)	0.7 (3.4)
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*NSAID* non-steroidal anti-inflammatory drug, *PPPY* per-patient-per-year, *SCD* sickle cell disease, *SD* standard deviation, *VOC* vaso-occlusive crisis

<sup>a</sup>Data were assessed during the variable-length follow-up, beginning on the index date and ending on the earliest date of either inpatient death, end of continuous enrollment, or end of the study period (March 1, 2020)

<sup>b</sup>Data are presented for all patients with SCD with recurrent VOCs

<sup>c</sup>Opioids included buprenorphine, dihydrocodeine, fentanyl, hydromorphone, morphine, oxycodone, tramadol, and Tylenol with codeine

**Supplementary Table 3** Annual HCRU for patients with SCD with recurrent VOCs by payer type<sup>a</sup>

	Patients with SCD with recurrent VOCs	
	Commercial ( <i>n</i> = 679)	Medicaid ( <i>n</i> = 2737)
Inpatient		
Patients with $\geq 1$ admission, <i>n</i> (%)	631 (92.9)	2577 (94.2)
Inpatient admissions PPPY, mean (SD)	2.4 (2.4)	2.7 (3.0)
Outpatient visits PPPY, mean (SD)		
All outpatient <sup>b</sup>	50.6 (49.2)	50.1 (47.8)
Emergency department <sup>c</sup>	4.0 (7.5)	5.3 (8.2)
Physician office <sup>d</sup>	11.1 (13.9)	11.2 (9.2)
Laboratory <sup>e</sup>	12.1 (12.2)	9.1 (8.5)
Other <sup>f</sup>	23.4 (30.6)	24.5 (36.8)
Outpatient pharmacy		
Prescriptions PPPY, mean (SD)	27.7 (22.6)	36.9 (29.3)

*HCRU* healthcare resource utilization, *PPPY* per-patient-per-year, *SCD* sickle cell disease, *SD* standard deviation, *VOC* vaso-occlusive crisis

<sup>a</sup>Data were assessed during the variable-length follow-up, beginning on the index date and ending on the earliest date of either inpatient death, end of continuous enrollment, or end of the study period (March 1, 2020)

<sup>b</sup>Outpatient visits were counted by identifying unique visits to a particular healthcare provider type on a particular date

<sup>c</sup>Emergency department visits were counted as the number of distinct dates with an emergency department claim

<sup>d</sup>Physician office visits were counted as the number of distinct dates with a visit to a unique healthcare provider type in an office setting

<sup>e</sup>Laboratory visits were counted as the number of distinct dates with a visit to a laboratory

<sup>f</sup>Other outpatient visits were counted as the number of distinct dates with a visit to a unique healthcare provider type in a non-office setting (e.g. radiology, outpatient surgery, etc.)