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Characterizing sickle cell disease and burden of illness in the United States of America: a retrospective analysis of real-world data

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KEY FINDINGS & CONCLUSIONS

- To our knowledge, this is the first documented use of physician notes complementing structured data to characterize sickle cell disease (SCD) in a real-world setting.
- We report a high level of healthcare consumption, predominantly involving specialist care and diagnostic procedures; only a small proportion of patients utilized outpatient-only care for vaso-occlusive crisis (VOC) management.
- Our findings emphasize the importance of preventing and minimizing VOCs.
- Importantly, we demonstrate the considerable contribution that physician notes can make to better characterizing disease manifestation in SCD.

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INTRODUCTION

- SCD continues to be a major global public health issue, with a prevalence of 1:365 in the black/African American population in the United States.[1]
- The hallmark of SCD is painful VOCs, which are associated with an increased risk of SCD-related organ damage and are the most common cause of hospitalization for patients with SCD.[2–4]
- Despite advances in screening, management, and treatment, gaps remain in our understanding of SCD in the real-world setting. Most observational studies of SCD rely on structured data (ie predefined clinical concepts such as International Classification of Diseases [ICD]-9/10 codes) from electronic medical records (EMRs); however, unstructured narrative sections of physician notes are often neglected despite being clinically relevant.
- Advances in data analytic methods allow for the combination of physician notes and structured data, potentially providing a more accurate and complete picture of disease manifestation.
- The aim of this study was to evaluate disease manifestation in terms of VOCs and SCD-related organ damage, as well as current management approaches, and to evaluate the clinically relevant information that can be captured from physician notes.

METHODS

- This retrospective, non-interventional, observational study enrolled 403 patients with confirmed SCD who had ≥1 hospitalization due to VOC (H-VOC) in the 12 months before recruitment. Patients were recruited through digital channels, patient ambassadors, and through a variety of partnerships (eg with healthcare providers, patient advocacy groups, and centers of excellence).
- Of the 403 enrolled patients, data were analyzed from 235 patients aged ≥16 years at the year of index date (ie the first day after the 12-month baseline observation period) and who had ≥1 year of follow-up data after the index date.
- The observation period (baseline plus follow-up) required ≥2 clinical document records ≥30 days apart and ≥1 clinical document every 6 months. Each patient's longest observation period was used for this analysis.
- Event rates are adjusted for exposure time (time between start and end date of observation period) and reported as rates per person-year with 95% confidence intervals (CIs).
- Human-curated natural language processing with assistance from machine learning algorithms was used to extract EMR data.[5]
- Conditions, procedures, and laboratory results were abstracted from standard, structured sections of the medical record. In addition, a specific set of SCD-related conditions and procedures were abstracted from physician notes.[5,6]
- Healthcare providers were grouped according to the International Standard Classification of Occupations (ISCO-08).

RESULTS

Demographics and baseline characteristics

- The median age (Q1–Q3) of the 235 patients included in this analysis was 29 years (23–35); 172 (73%) patients were female, 160 (68%) patients had the HbSS genotype of SCD, and 216 (92%) patients were black or African American (**Table 1**).

Table 1. Patient demographics.

Demographic	Patients (N=235)
Age, years, median (Q1–Q3)	29 (23–35)
Sex, n (%)	
Female	172 (73)
Male	63 (27)
SCD genotype, n (%)	
HbSS	160 (68)
HbSC	39 (17)
HbSβ+	23 (10)
HbSβ0	5 (2)
Other	2 (1)
Unknown	6 (3)
Race, n (%)	
Black or African American	216 (92)
Other (white or prefer not to say)	5 (2)
Missing	14 (6)

SCD, sickle cell disease

- During the baseline period, 102 (43%) patients had ≥1 H-VOC (including emergency department visits) (**Table 2**).
- 88 (37%) patients had ≥1 outpatient VOC, and 32 (14%) had been hospitalized due to comorbidities primarily related to bone necrosis (9%) and pulmonary disease (8%) (**Table 2**).

Table 2. Baseline characteristics.

Characteristic	Patients (N=235)
VOCs	
History of H-VOC,* n (%)	102 (43)
Visits, median (Q1–Q3)	2 (1–5)
History of outpatient VOC, n (%)	88 (37)
Visits, median (Q1–Q3)	2 (1–4)
Treatment history† at baseline	
Supportive treatments,‡ n (%)	182 (77)
Opioids	177 (75)
Non-opioid analgesics	156 (66)
Antidepressants	38 (16)
Anxiolytics	22 (9)
HU, n (%)	114 (49)
Blood transfusions, n (%)	41 (17)
Visits, median (Q1–Q3)	2 (1–3)
0	194 (83)
1–5 (ie rescue)	40 (17)
≥6 (ie chronic)	1 (<1)
Hospitalization due to comorbidities	
All comorbidities,§ n (%)	32 (14)
Bone necrosis	21 (9)
Pulmonary disease	18 (8)
CNS disease	3 (1)
Cardiac disease	2 (1)

*In total there were 452 hospitalizations, of which 136 were standalone emergency department (ED) visits, 125 involved the ED and 191 did not involve the ED; †Received in the first 12 months of the observational period, prior to the follow-up period; ‡Administered to treat symptoms, rather than underlying disease mechanism; §Top four reasons for hospitalization due to comorbidities are shown; other comorbidities observed (n [%]) included leg ulcer and splenic dysfunction (1 [<1] for both)
CNS, central nervous system; HU, hydroxyurea; H-VOC, hospitalization due to VOC; SCD, sickle cell disease; VOC, vaso-occlusive crisis

Disease progression during follow-up

- During follow-up (median [Q1–Q3] of 3.6 [2.1–6.0] years), 218 (93%) patients experienced ≥1 VOC (H-VOC rate [95% CI] of 4.25 [3.64–4.95] per person-year; outpatient VOC rate [95% CI] of 2.39 [1.97–2.91] per person-year) and 143 (61%) were hospitalized for SCD-related organ damage (rate of 0.97 [0.79–1.21] per person-year) (**Figure 1**).

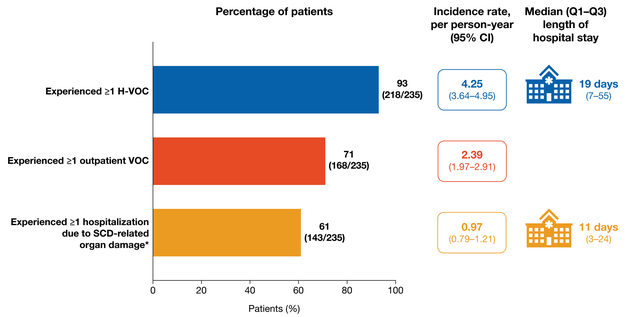

Figure 1. Proportion of patients who experienced ≥1 H-VOC, outpatient VOC, or hospitalization due to SCD-related organ damage.

Data labels are % (n/N)
*SCD-related organ damage included bone necrosis, priapism, retinopathy and retinal disorder, pulmonary disease, renal disease, liver disease, CNS disease, leg ulcer, gallbladder disease, splenic dysfunction, and cardiac disease
CI, confidence interval; CNS, central nervous system; H-VOC, hospitalization due to VOC; SCD, sickle cell disease; VOC, vaso-occlusive crisis

Source of visit records

- In the baseline period, 285 (63%) H-VOCs, 194 (83%) outpatient VOCs, and 68 (80%) hospitalizations due to SCD-related organ damage were extracted exclusively from physician notes (**Table 3**).
- During the follow-up period, 764 (19%) H-VOCs, 1351 (52%) outpatient VOCs, and 423 (50%) hospitalizations due to SCD-related organ damage were extracted exclusively from physician notes (**Table 3**).

Table 3. Source of visit records.

	Total records, N	Records from both portions of EMR, n (%)	Records from physician notes only, n (%)	Records from structured data only, n (%)
Baseline				
Source of baseline visit records				
H-VOC	452	167 (37)	285 (63)	0 (0)
Outpatient VOC	234	37 (16)	194 (83)	3 (1)
Hospitalization due to SCD-related organ damage	85	17 (20)	68 (80)	0 (0)
Top four reasons for hospitalization due to SCD-related organ damage*				
Bone necrosis	58	6 (10)	52 (90)	0 (0)
Pulmonary disease	32	1 (3)	30 (94)	1 (3)
CNS disease	6	0 (0)	6 (100)	0 (0)
Leg ulcer	3	3 (100)	0 (0)	0 (0)
Follow-up				
Source of follow-up visit records				
H-VOC	3945	3082 (78)	764 (19)	99 (3)
Outpatient VOC	2585	1191 (46)	1351 (52)	43 (2)
Hospitalization due to SCD-related organ damage	854	391 (46)	423 (50)	40 (5)
Top four reasons for hospitalization due to SCD-related organ damage†				
Bone necrosis	409	127 (31)	251 (61)	31 (8)
Pulmonary disease	357	101 (28)	236 (66)	20 (6)
CNS disease	75	8 (11)	60 (80)	7 (9)
Priapism	51	30 (59)	21 (41)	0 (0)

*Other SCD-related organ damage observed (total records [N]) included cardiac disease (2) and splenic dysfunction (1); †Other SCD-related organ damage observed (total records [N]) included splenic dysfunction (35), retinopathy and retinal disorder (23), renal disease (19), cardiac disorder (15), liver disease (4), and gallbladder disease (3)
CNS, central nervous system; EMR, electronic medical record; H-VOC, hospitalization due to VOC; SCD, sickle cell disease; VOC, vaso-occlusive crisis

Healthcare consumption

- The overall diagnostic procedure rate per person-year (95% CI) was 20.36 (18.54–22.36), with blood tests, X-rays, and urinalysis being the most common (**Figure 2**).

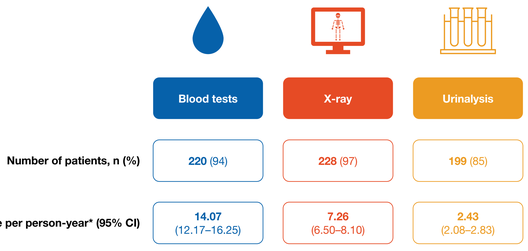

Figure 2. Top three diagnostic procedures in the follow-up period.

*Rates are adjusted for exposure time. Procedures included X-ray, computerized tomography, magnetic resonance imaging, ultrasonography, ultrasound, echocardiography, transcranial Doppler, Doppler echocardiography, electrocardiographic monitoring, blood testing including hemoglobin electrophoresis, high-performance liquid chromatography, DNA (gene) testing, complete blood count and reticulocyte count, serum electrolytes, and urinalysis
CI, confidence interval

- In total, 224 (95%) patients received supportive treatments, which included opioids (95%), non-opioid analgesics (92%), antidepressants (40%), and anxiolytics (33%). In total, 183 (78%) patients received HU and 119 (51%) patients received blood transfusions.
  - The blood transfusion rate per person-year (95% CI) was 0.99 (0.77–1.27).
- Patients mostly visited (ie inpatient and outpatient visits, and visits related to diagnostic procedures and treatment) specialist medical practitioners (rate per person-year [95% CI] of 15.46 [13.73–17.40]), while relatively few visited general medical practitioners (rate per person-year [95% CI] of 1.72 [1.46–2.02]) (**Figure 3**).

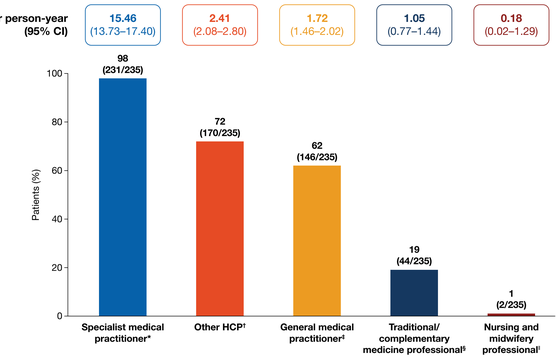

Figure 3. Healthcare provider visits in the follow-up period.

Data labels are % (n/N)
*Top six providers, n (%): radiology, 226 (98); emergency medicine, 188 (81); cardiology, 160 (69); internal medicine, 159 (69); hematology/oncology, 154 (67); hospital medicine, 125 (54); †Top six providers, n (%): missing/not provided, 166 (98); pharmacology, 19 (11); physical therapy, 15 (9); psychology, 5 (3); occupational therapy, 5 (3); dentistry, 4 (2); ‡Providers, n (%): family medicine, 145 (99); general practice, 2 (1); §Top six providers, n (%): nutrition, 34 (77); social work, 27 (62); music therapy, 2 (5); massage therapy, 2 (5); wound care, 1 (2); social worker, 1 (2); ‖Provider, n (%): nurse practitioner, 2 (100)
CI, confidence interval; HCP, healthcare professional

Discussion and limitations

- The recruitment of individuals in this real-world cohort included a weighting towards patients with more severe SCD, including only those with ≥1 H-VOC in the 12 months preceding recruitment. This may have led to sampling bias, resulting in a cohort that is biased toward patients with more severe SCD with known hospitalizations, and less reflective of the larger, more heterogeneous SCD population.
- A variable including the certainty of the record was included, and records with low certainty were excluded. Several measures were in place to ensure the quality of the data from physician notes.
- Only medical conditions and procedures related to SCD were abstracted from the physician notes.
- No sensitivity or subgroup analyses were conducted due to a limited sample size.

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Disclosures

E Leila Jerome Clay reports receiving consultancy fees from Novartis and GBT. **Christopher Rowe** and **Meghan Tierney** are employees of, and holders of stock options in, PicnicHealth. **Yun Zhou** is an employee of Genesis Research. **Jincy Paulose, Thirupathi Pattipaka, David Wormser,** and **Jilles M Fermont** are employees of Novartis.

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