# Clinical and Social Determinants of Health as Risk-Factors of End-Organ Damage in Sickle Cell Disease: A Retrospective Analysis

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## Background

Sickle cell disease (SCD) is a chronic, inherited blood disorder marked by the sickling of red blood cells and hemoglobin deoxygenation. These abnormalities can lead to progressive end-organ damage, affecting the lungs, brain, kidneys, and bones.[1] Despite advancements in SCD care, patients continue to face significant health disparities and complex challenges. To address these unmet needs, the American Society of Hematology has identified key research priorities, including the prevention and treatment of end-organ dysfunction, as a focus for the next five years.[2]

## Objective

Leveraging real-world data from electronic health records (EHR) and CDC reports, this analysis evaluates how hemoglobin (Hb) levels, comorbidities, and social vulnerability factors relate to end-organ damage (EOD) in patients with sickle cell disease.

## Methodology

**Data Source**
Retrospective analysis of EHR data from January 2018 to December 2024

**Patient Identification**
- Identify patients with sickle cell anemia using ICD diagnosis codes
- **Inclusion criteria:** patient has recorded hemoglobin levels within -3 to +6 months of the first SCD diagnosis AND patient has at least two EHR encounters within 12 months after the first SCD diagnosis to ensure data continuity **(N = 1,826 patients)**

**Independent Variables Measurement**
- Social determinants of health measured with CDC-derived Social Vulnerability Index (SVI)[3]
- Comorbidities assessed with Charlson Comorbidity Index (CCI)[4] derived from EHR data
- Hemoglobin levels recorded within -3 to +6 months of first SCD diagnosis in EHR data

**Outcome Measurement**
Patients were followed post-diagnosis to estimate onset of EOD, specifically: chronic kidney disease, pulmonary hypertension, stroke, and leg ulcers

**Statistical Analysis**
Multivariable generalized estimating equations (GEE) applied to estimate associations between independent variables (Hb, SVI, CCI) and risk of developing EOD

**Table 1:** Patient Cohort Characteristics

| Characteristic, n (%) | Total (n = 1,826) |
|---|---|
| Gender | |
| Female | 1,198 (66%) |
| Male | 628 (34%) |
| Race and Ethnicity | |
| White Not Hispanic | 1,020 (56%) |
| White Hispanic | 61 (3%) |
| Black | 290 (16%) |
| Asian | 8 (0.4%) |
| Unknown | 447 (12%) |

| Characteristic, n (%) | Total (n = 1,826) |
|---|---|
| Age category, years | |
| <= 17 | 200 (11%) |
| 18 - 34 | 741 (41%) |
| 34 – 44 | 329 (18%) |
| 45-54 | 243 (13%) |
| 55-64 | 171 (9%) |
| 65>= | 142 (8%) |

**Table 2:** Association of Clinical and Social Variables with End-Organ Damage in SCD Patients

| Variable | Odds Ratio | 95% CI | p-value | Interpretation |
|---|---|---|---|---|
| log (SVI) | 2.14 | [1.43, 3.20] | < 0.0001 | Each 1-unit increase in log(SVI), which corresponds to a two-fold increase in SVI (e.g., SVI increasing from 0.2 to 0.4), is associated with a 2.14x increase in the odds of EOD. |
| CCI | 1.53 | [1.38, 1.70] | < 0.0001 | Each 1-point increase in CCI increases the odds of EOD by 53%. |
| Hb 7-8 g/dL | 0.52 | [0.46, 0.60] | < 0.0001 | Patients with Hb of 7-8 g/dL have 48% lower odds of EOD. |
| Hb 8-9 g/dL | 0.41 | [0.37, 0.48] | < 0.0001 | Patients with Hb of 8-9 g/dL have 59% lower odds of EOD. |
| Hb 9-10 g/dL | 0.35 | [0.31, 0.41] | < 0.0001 | Patients with Hb of 9-10 g/dL have 65% lower odds of EOD. |
| Hb 10-11 g/dL | 0.26 | [0.23, 0.32] | < 0.0001 | Patients with Hb of 10-11 g/dL have 74% lower odds of EOD. |
| Hb 11-12 g/dL | 0.19 | [0.16, 0.23] | < 0.0001 | Patients with Hb of 11-12 g/dL have 79% lower odds of EOD. |
| Hb >12 g/dL | 0.15 | [0.12, 0.19] | < 0.0001 | Patients with Hb >12 g/dL have 85% lower odds of EOD. |

*All variables show acceptable multicollinearity, with VIFs mostly between 1.10–1.17 and log(SVI) at 1.7.

**Figure 1**: Probability of End Organ Damage by Hemoglobin Levels and Comorbidity Burden

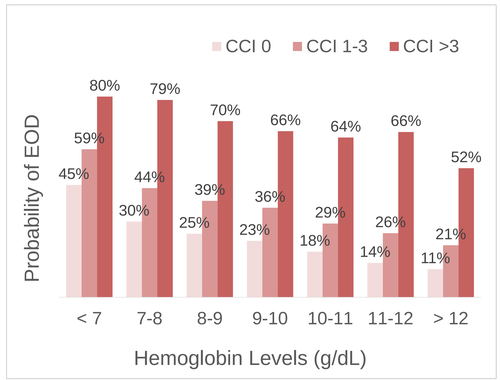
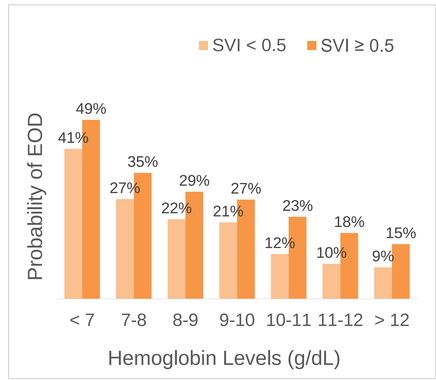



**Figure 2**: Probability of End Organ Damage by Hemoglobin Levels and Social Vulnerability




## Results

- Among 1,826 sickle cell disease patients with measured hemoglobin levels, end-organ damage was observed in 331 cases (18%).
- Higher hemoglobin levels are associated with lower EOD risk in SCD patients, with odds decreasing progressively – from 48% lower odds in the 7-8 g/dL group to 85% lower odds in those with > 12 g/dL (Table 2).
- A two-fold increase in SVI is associated with a 2.14x increase on odds of EOD, and each 1-point increase in CCI corresponds to a 53% higher odds of EOD while holding all other variables constant (Table 2).
- For patients with similar Hb levels, EOD probability increased along with clinical and social risk factors.
  - Hb < 7 g/dL: patients with high comorbidity burden (CCI > 3) have a higher EOD probability of 80%, versus 45% for CCI = 0; those more socially vulnerable (SVI ≥ 0.5) have a higher EOD probability of 49%, versus 41% for SVI < 0.5.
  - Hb > 12 g/dL: those with high comorbidity burden (CCI > 3) have a higher EOD probability of 52%, versus 11% for CCI = 0; more socially vulnerable (SVI ≥ 0.5) have higher EOD probability at 15%, versus 9% for SVI < 0.5.
  - Similar patterns are seen across intermediate Hb levels (7-12 g/dL).

## Conclusion

Our analysis suggests that both clinical factors and social determinants of health could play a role in sickle cell disease progression and end-organ damage. While traditional health systems emphasize SCD's biomedical burden,[5] a deeper understanding of the relationship between social risk factors and sickle cell progression could support a more holistic approach to risk stratification and care management by integrating both clinical and social drivers.

## Limitation and Future Considerations

- This analysis is limited to patients captured in Compile's EHR data.
- Future analyses may assess the impact of individual SDoH factors (e.g., patient net worth, race/ethnicity) as standalone variables.
- Incorporating interaction terms across key EOD-contributing factors (e.g., social vulnerability × hemoglobin levels) may help uncover compounding risks and clarify the relative contribution of each variable.

### References; Footnotes

1) Ershler WB, De Castro LM, Pakbaz Z, Moynahan A, Weycker D, Delea TE, Agodoa I, Cong Z. Hemoglobin and End-Organ Damage in Individuals with Sickle Cell Disease. Curr Ther Res Clin Exp. 2023;98:100696. doi:10.1016/j.curtheres.2023.100696.
2) American Society of Hematology. ASH Announces Sickle Cell Disease Research Priorities. Published January 25, 2024. Accessed May 1, 2025. https://www.hematology.org/newsroom/press-releases/2024/ash-announces-sickle-cell-disease-research-priorities
3) SVI is derived by the CDC across four themes: socioeconomics status, household characteristics, race & ethnicity, housing type & transportation. SVI is calculated on a ZIP5 level, and each patient's ZIP5 is assigned based on the pharmacy or hospital they most frequently visit, as identified in Compile claims data.
4) 347 out of 1,826 patients in our cohort have diagnoses that qualify for a CCI score (CCI > 0), based on a one-year lookback period and occurring within one year of their first SCD diagnosis.
5) DeBaun MR. To Address the Fragility of the Sickle Cell Disease Community, Prioritize the Social Determinants of Health. Am J Hematol. 2020;95(8):E198–E200. doi:10.1002/ajh.25837.