

Economic Burden Associated with Managing Patients with Sickle Cell Disease Receiving Frequent Red Blood Cell Transfusions in the United States

Chuka Udeze¹; Michelle Jerry²; Kristin Evans²; Nanxin Li¹; **Siddharth Jain¹**; Biree Andemariam³

¹Vertex Pharmaceuticals Incorporated, Boston, MA, USA, ²Merative, Ann Arbor, MI, USA, ³University of Connecticut Health, Farmington, CT, USA

BACKGROUND

- Sickle cell disease (SCD) is a rare genetic disorder characterized by abnormal sickle hemoglobin, which leads to vaso-occlusive crises (VOCs) and a variety of other acute and chronic complications.^{1–4}
- Standard of care for patients with SCD includes hydroxyurea and red blood cell transfusions (RBCTs) in addition to supportive care.⁵
- Some patients with SCD receive frequent RBCTs which can alleviate some symptoms and reduce the risk of developing additional SCD-related complications.⁶ Data on outcomes in this specific population are limited.

OBJECTIVE

- To describe clinical and economic outcomes of patients with SCD receiving frequent RBCTs in the United States.

METHODS

Study Design and Database

- This longitudinal, retrospective analysis used the Merative™ MarketScan® Databases to identify patients with SCD with frequent RBCTs during any 12-month period between January 1, 2015 and February 29, 2020.
- The MarketScan Databases contain de-identified inpatient medical, outpatient medical, and outpatient prescription drug data for ~198.9 million commercially insured individuals and their dependents between 1995 and 2020, ~14.4 million Medicare Supplemental individuals between 1995 and 2020, and ~52 million Medicaid enrollees between 1999 and 2020.

Patient Identification

- Patients were included in the analysis if they met the following key inclusion criteria:
 - ≥1 inpatient or ≥2 outpatient claims with a diagnosis of SCD between January 1, 2015 and March 1, 2019
 - ≥6 RBCT claims (at least 3 days apart) during any 12-month period after the earliest qualifying SCD diagnosis; the date of the 6th RBCT is the index date
 - ≥12 months of continuous enrollment before and after the index date
- Patients were excluded if they met the following exclusion criteria:
 - Evidence of hematopoietic stem cell transplant or sickle cell trait at any point in the study period
- All patients were followed for ≥12 months, 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 (February 29, 2020).

Study Measures and Analysis

- Descriptive analyses were conducted for all outcomes for patients with SCD receiving frequent RBCTs.
 - Mean (standard deviation [SD]) values were reported for continuous variables and frequencies/proportions (n,%) for categorical variables.
- Demographics including age, sex, and payer type were assessed at the index date.
- Annualized rates (per patient per year [PPPY]) of all-cause healthcare resource utilization (HCRU) included inpatient admissions, outpatient visits, and outpatient prescriptions.
- Annualized rates of VOCs and RBCTs were characterized separately.
- Annualized healthcare costs, comprised of inpatient, outpatient medical, and outpatient prescription costs, were based on the paid amounts of adjudicated claims, including payer and health plan payments, as well as patient cost-sharing in the form of co-payment, deductible, and co-insurance.
- Costs were inflated to 2022 United States Dollars using the Medical Care Component of the Consumer Price Index.

Subgroups – Baseline VOCs & RBCT Frequency During Follow-Up

- Two subgroup analyses were conducted based on number of VOCs during the 12-month baseline (<2 VOCs, ≥2 VOCs) and consistency of transfusions in the follow-up period (≥6 RBCTs during each year of the follow-up period).

RESULTS

Patient Demographics

- In total, 919 patients with SCD receiving frequent RBCTs met inclusion criteria (**Figure 1**).
- Mean (SD) age of patients with SCD with frequent RBCTs was 19.5 (13.3) years (**Table 1**).
- The majority (78.5%) of patients included in the study were captured in the Medicaid database (**Table 1**).

Figure 1. Patient Selection

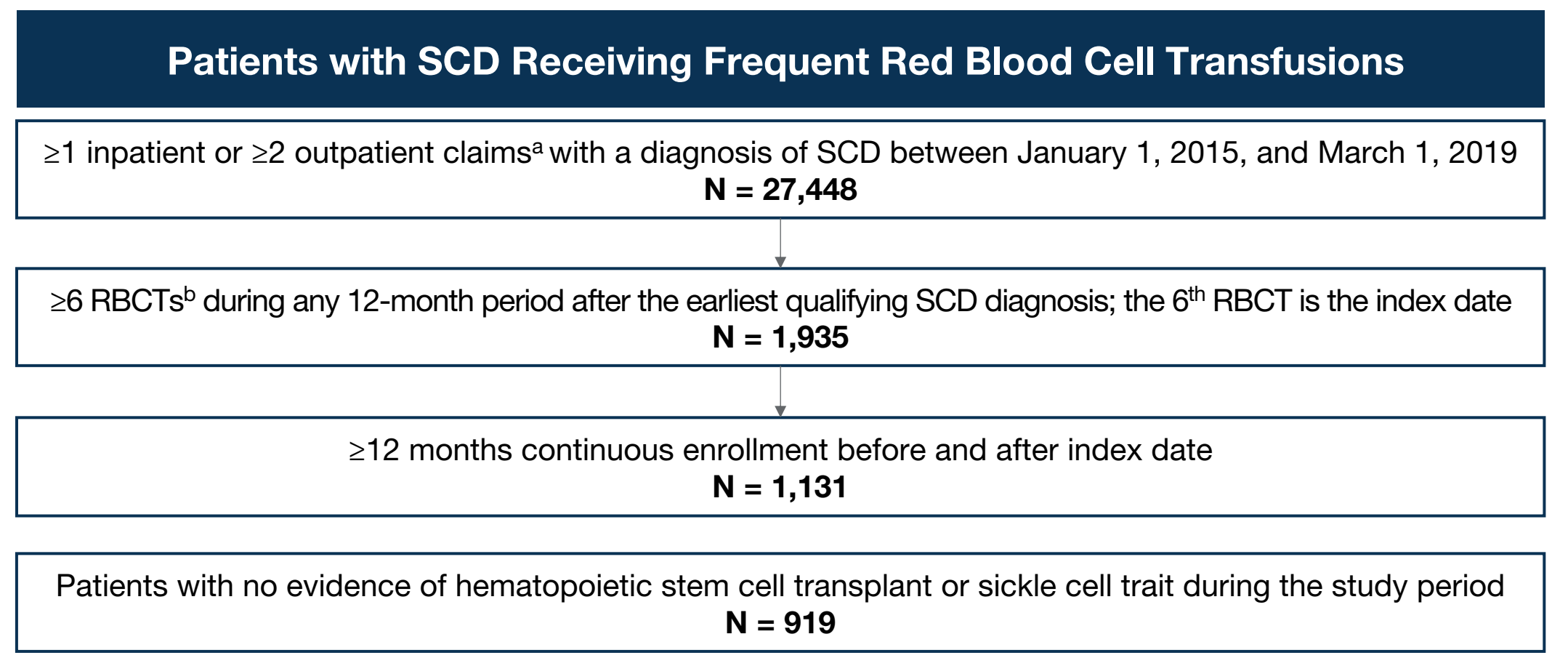


Table 1. Patient Demographics

	SCD with Frequent RBCTs (n = 919)
Age, mean (SD, min–max), years	19.5 (13.3, 0–73)
Sex, n (%)	
Female	466 (50.7)
Male	453 (49.3)
Payer Type, n (%)	
Commercial	195 (21.2)
Medicare Supplemental	3 (0.3)
Medicaid	721 (78.5)
Medicaid fee for service (FFS)	370 (40.3)
Years of follow-up, mean (SD)	3.1 (1.2)

Abbreviations: SCD: sickle cell disease; RBCTs: red blood cell transfusions.

HCRU and Costs

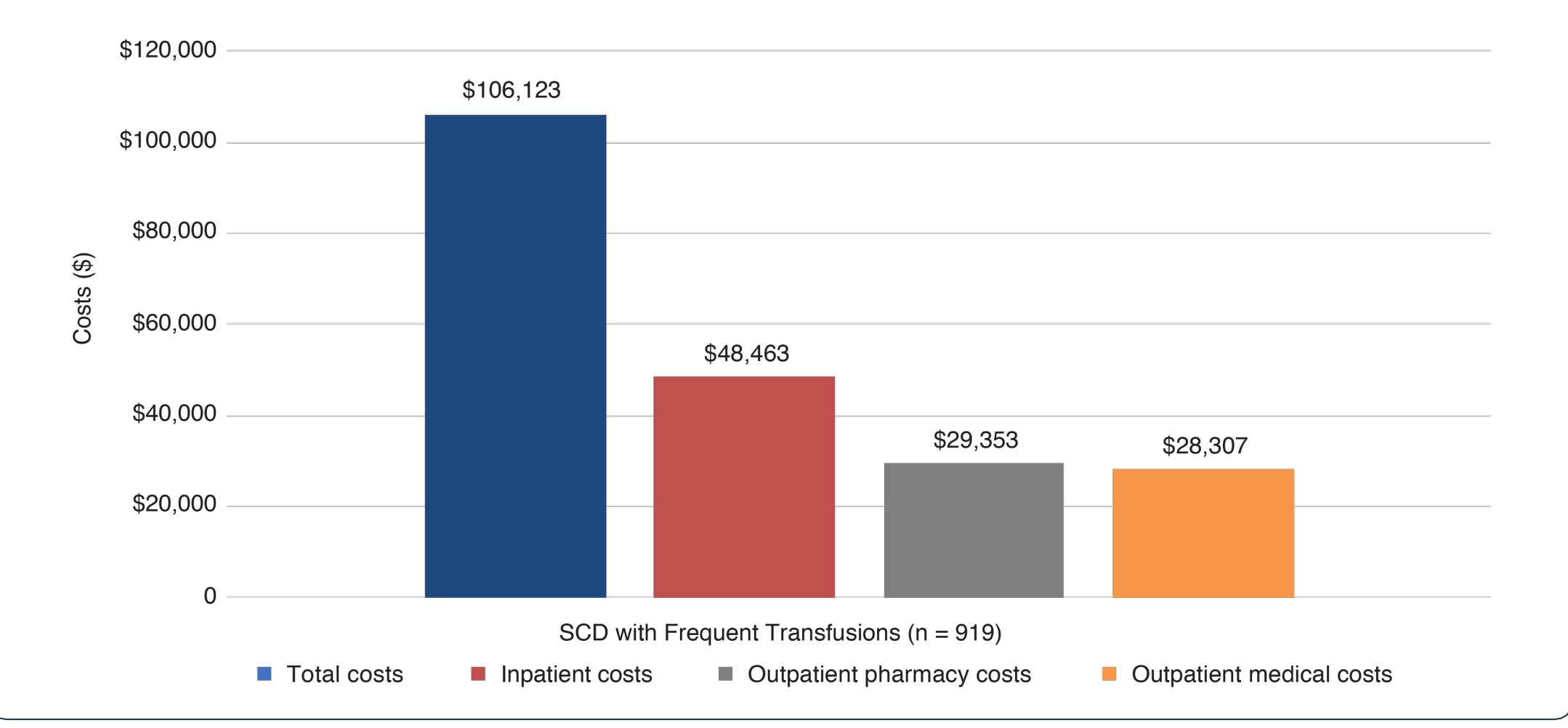
- Patients with SCD receiving frequent RBCTs experienced a mean (SD) of 4.0 (8.2) VOCs PPPY and received 8.3 (4.0) RBCTs PPPY during the follow-up period.
- Patients had a mean (SD) of 2.3 (3.7) inpatient admissions, 83.5 (71.4) outpatient visits, 4.4 (14.1) emergency department visits, and 37.4 (33.4) outpatient prescriptions PPPY during follow-up (**Table 2**).
- Mean (SD) total healthcare costs for patients with SCD receiving frequent RBCTs were \$106,123 (\$130,534) PPPY (**Figure 2**).
 - Mean inpatient, outpatient pharmacy, and outpatient costs were \$48,463 (\$116,732), \$29,353 (\$41,670), and \$28,307 (\$37,670), respectively, during the follow-up period (**Figure 2**).

Table 2. Annual Healthcare Resource Utilization

Utilization Per Patient Per Year	SCD with Frequent RBCTs (n = 919)
Inpatient	
Number of admissions, mean (SD)	2.3 (3.7)
Days of hospitalization, mean (SD)	12.6 (23.5)
Outpatient	
Total number of visits, mean (SD) ^a	83.5 (71.4)
Emergency department visits, mean (SD)	4.4 (14.1)
Office visits, mean(SD) ^b	15.9 (10.9)
Laboratory visits, mean (SD) ^c	21.3 (13.3)
Other outpatient visits, mean (SD) ^d	41.9 (59.7)
Outpatient pharmacy	
Number of prescriptions, mean (SD)	37.4 (33.4)
Red Blood Cell Transfusions^e	
Number of RBCTs, mean (SD)	8.3 (4.0)

^aOutpatient visits – Denoted as a patient, seeing a distinct provider type (e.g., primary care, podiatrist, etc), on a distinct date. Emergency department visits, outpatient office visits, laboratory visits, and other outpatient visits are included in this total.
^bOutpatient office visit – Denoted as a patient visiting an office setting, at a unique provider type, on a distinct date (e.g., visits usually associated with being evaluated/managed by a physician)
^cLaboratory visits – Denoted as a patient visiting a lab setting, at a unique provider type, on a unique date
^dOther outpatient visits – Denoted as a patient visiting a non-office outpatient setting, at a unique provider type, on a unique date (e.g., visits for screening, x-ray, transfusions, intravenous iron chelation administration, etc)
^eNumber of RBCTs are not mutually exclusive from inpatient and outpatient categorizations; visits for RBCTs could also be captured in other healthcare resource utilization categories
Abbreviations: SCD: sickle cell disease; RBCTs: red blood cell transfusions.

Figure 2. Mean Annual Costs



Subgroup Analyses – Number of VOCs at Baseline

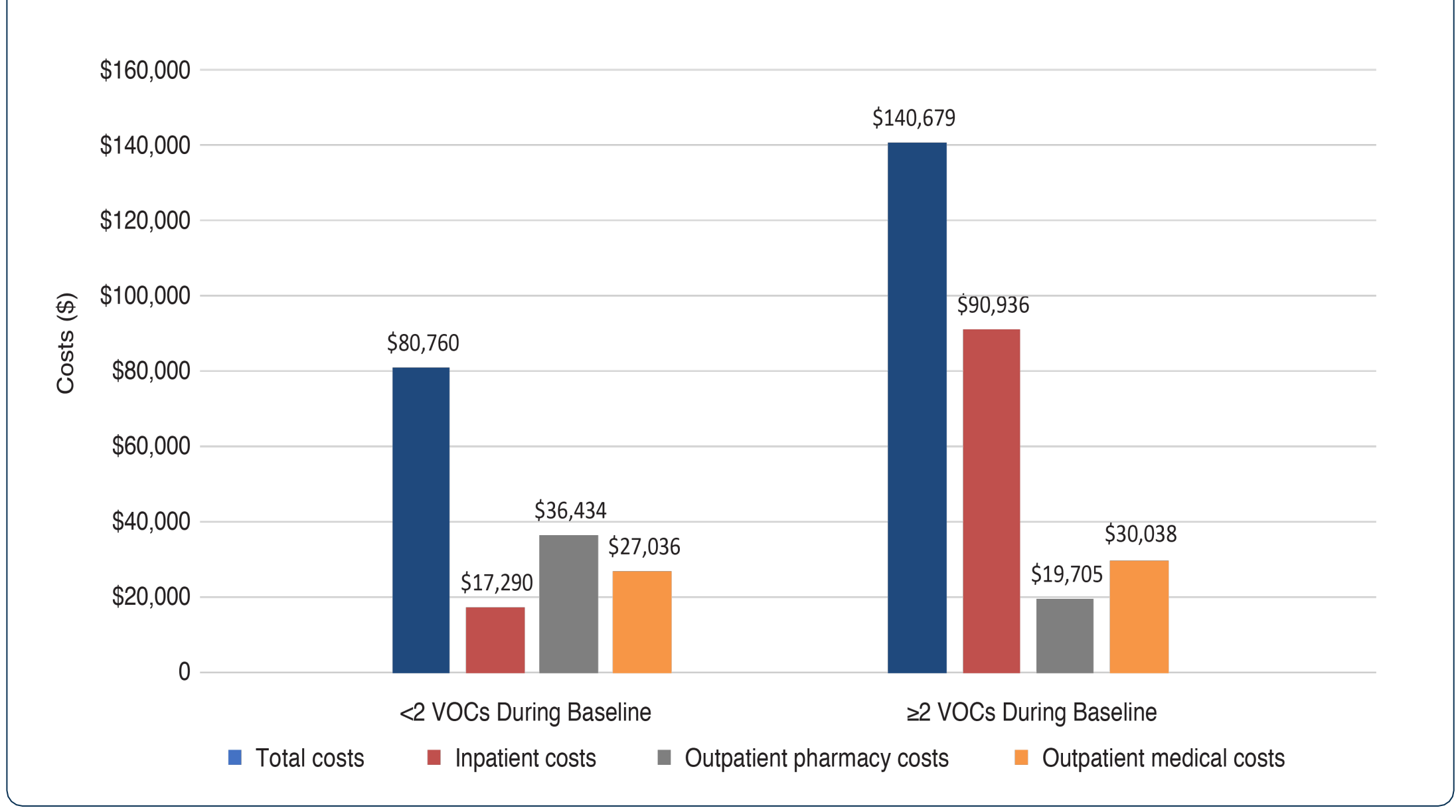
- Patients with ≥2 VOCs during baseline had a higher mean [SD] rate of VOCs per year during follow-up, compared to patients with <2 baseline VOCs (8.4 [11.1] vs 0.8 [1.3]) and a lower mean [SD] rate of RBCTs (7.0 [4.1] vs 9.3 [3.7]).
- Patients with ≥2 VOCs during baseline had substantially higher annual mean [SD] HCRU (**Table 3**) and total healthcare costs, compared to patients with <2 baseline VOCs (\$140,679 [\$171,581] vs \$80,760 [\$80,331]) (**Figure 3**).

Table 3. Annual Healthcare Resource Utilization by Number of Baseline VOCs

Utilization Per Patient Per Year	<2 VOCs During Baseline (n = 530)	≥2 VOCs During Baseline (n = 389)
Inpatient		
Number of admissions, mean (SD)	0.7 (1.1)	4.5 (4.7)
Days of hospitalization, mean (SD)	3.4 (7.0)	25.2 (31.1)
Outpatient		
Total number of visits, mean (SD) ^a	76.3 (61.0)	93.4 (82.6)
Emergency department visits, mean (SD)	1.5 (2.6)	8.4 (20.8)
Office visits, mean (SD) ^b	15.1 (9.5)	16.9 (12.5)
Laboratory visits, mean (SD) ^c	21.9 (11.9)	20.4 (14.9)
Other outpatient visits, mean (SD) ^d	37.7 (54.3)	47.7 (65.9)
Outpatient pharmacy		
Number of prescriptions, mean (SD)	29.4 (26.0)	48.2 (39.0)
Red Blood Cell Transfusions^e		
Number of RBCTs, mean (SD)	9.3 (3.7)	7.0 (4.1)

^aOutpatient visits – Denoted as a patient, seeing a distinct provider type (e.g., primary care, podiatrist, etc), on a distinct date. Emergency department visits, outpatient office visits, laboratory visits, and other outpatient visits are included in this total.
^bOutpatient office visit – Denoted as a patient visiting an office setting, at a unique provider type, on a distinct date (e.g., visits usually associated with being evaluated/managed by a physician)
^cLaboratory visits – Denoted as a patient visiting a lab setting, at a unique provider type, on a unique date
^dOther outpatient visits – Denoted as a patient visiting a non-office outpatient setting, at a unique provider type, on a unique date (e.g., visits for screening, x-ray, transfusions, intravenous iron chelation administration, etc)
^eNumber of RBCTs are not mutually exclusive from inpatient and outpatient categorizations; visits for RBCTs could also be captured in other healthcare resource utilization categories
Abbreviations: SCD: sickle cell disease; RBCTs: red blood cell transfusions.

Figure 3. Mean Annual Costs by Number of Baseline VOCs



Subgroup Analyses – Patients with ≥6 RBCTs during each year of follow-up

- There was a lower mean [SD] rate of VOCs among patients who received ≥6 RBCTs during each year of the follow-up period (n=491) compared to the overall (n=919) patient population (2.4 [5.6] vs 4.0 [8.2]), and a higher mean [SD] rate of RBCTs (11.2 [2.5] vs 8.3 [4.0]) (**Table 4**).

Table 4. Annual Healthcare Resource Utilization by Number of RBCTs During Each Year of Follow-up

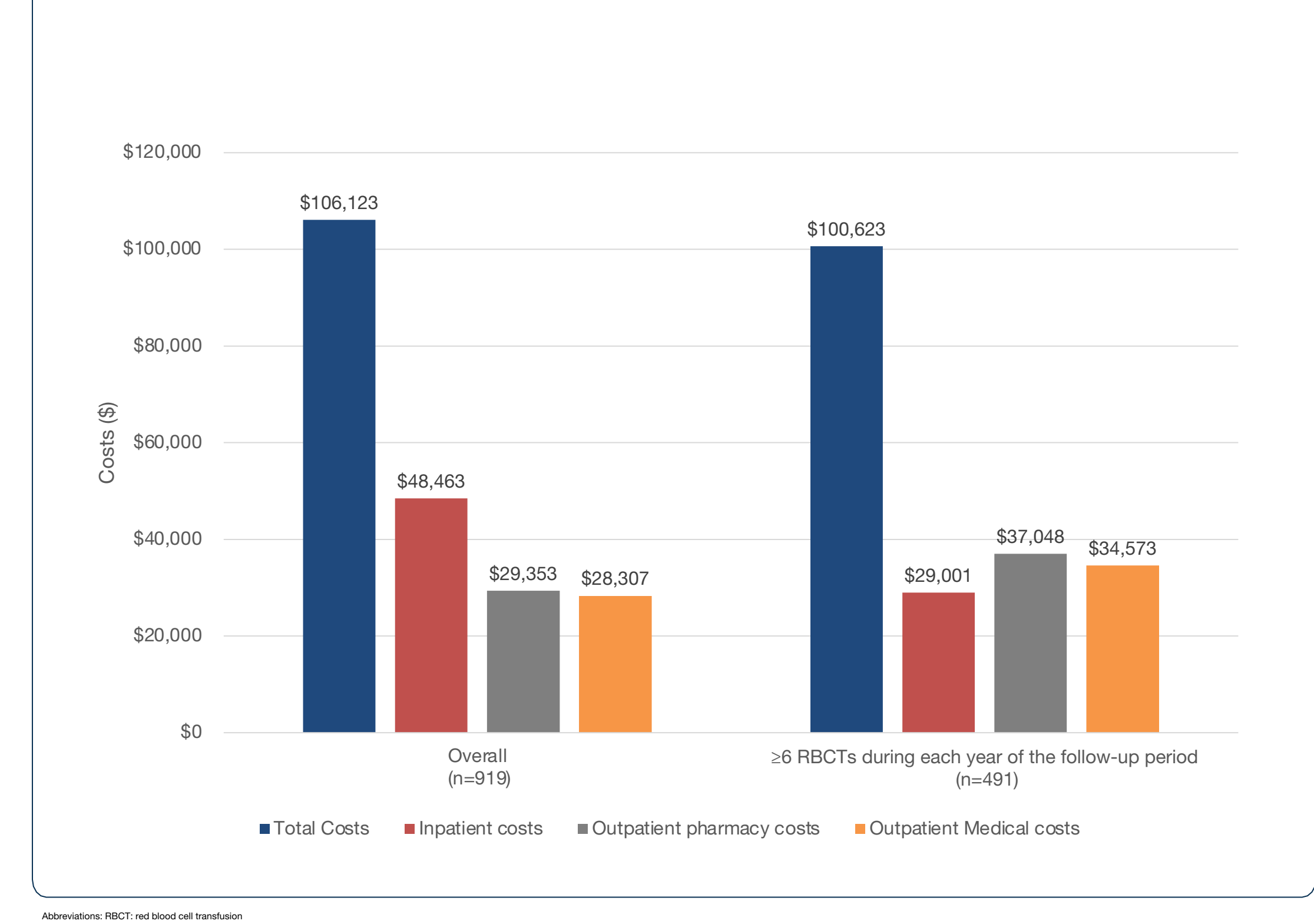
Utilization Per Patient Per Year	SCD with Frequent RBCTs (n = 919)	≥6 RBCTs During Each Year of Follow-up (n=491)
Inpatient		
Number of admissions, mean (SD)	2.3 (3.7)	1.5 (3.0)
Days of hospitalization, mean (SD)	12.6 (23.5)	8.0 (19.0)
Outpatient		
Total number of visits, mean (SD) ^a	83.5 (71.4)	91.0 (67.1)
Emergency department visits, mean (SD)	4.4 (14.1)	3.1 (9.8)
Office visits, mean (SD) ^b	15.9 (10.9)	17.5 (11.7)
Laboratory visits, mean (SD) ^c	21.3 (13.3)	25.7 (13.5)
Other outpatient visits, mean (SD) ^d	41.9 (59.7)	44.8 (54.6)
Outpatient pharmacy		
Number of prescriptions, mean (SD)	37.4 (33.4)	34.1 (35.4)
Red Blood Cell Transfusions^e		
Number of RBCTs, mean (SD)	8.3 (4.0)	11.2 (2.5)

^aOutpatient visits – Denoted as a unique patient, seeing a distinct provider type (e.g., primary care, podiatrist, etc), on a distinct date. Emergency department visits, outpatient office visits, laboratory visits, and other outpatient visits are included in this total.
^bOutpatient office visit – Denoted as a patient visiting an office setting, at a unique provider type, on a distinct date (e.g., evaluation and management visits with a physician)
^cLaboratory visits – Denoted as a patient visiting a lab setting, at a unique provider type, on a unique date
^dOther outpatient visits – Denoted as a patient visiting a non-office outpatient setting, at a unique provider type, on a unique date (e.g., visits for screening, x-ray, transfusions, IV iron chelation administration, etc)
^eNumber of RBCTs are not mutually exclusive from inpatient and outpatient categorizations; visits for RBCTs could also be captured in other healthcare resource utilization categories
Abbreviations: RBCTs: red blood cell transfusions; SCD: sickle cell disease; VOC: vaso-occlusive crises.

Subgroup Analyses – Patients with ≥6 RBCTs during each year of follow-up (continued)

- Patients who received ≥6 RBCTs during each year of the follow-up period had similar mean [SD] total healthcare costs as the overall population (\$100,623 [\$105,905] vs \$106,123 [\$130,534]).
- Mean [SD] inpatient costs were lower in the subgroup of patients receiving ≥6 RBCTs during each year of the follow-up period, compared to the overall population (\$29,001 [\$78,462] vs \$48,463 [\$116,732]), but outpatient costs (\$34,573 [\$42,702] vs \$28,307 [\$37,670]) and outpatient pharmacy costs (\$37,048 [\$48,894] vs \$29,353 [\$41,670]) were higher (**Figure 4**).

Figure 4. Mean Annual Costs Among Patients with ≥6 RBCTs During Each Year of Follow-Up



LIMITATIONS

- This study used administrative claims data collected for reimbursement purposes and is therefore subject to potential misclassification bias; only direct costs are included in this analysis, which likely underestimate the overall costs associated with SCD.
- Administrative claims databases capture insurer paid amounts and associated patient cost-sharing, which might underestimate the full cost of care to the healthcare system.
- Number of units per transfusion event are not able to be captured in administrative claims databases and thus the overall transfusion volume was not able to be assessed in this analysis.
- Individuals who died, went on long-term disability, or otherwise did not meet enrollment criteria may have systematically different outcomes than patients who met enrollment criteria.

CONCLUSIONS

- Patients with SCD that receive frequent RBCTs experience frequent VOCs and high annual healthcare costs.
- Patients with more VOCs at baseline experienced greater HCRU and higher total costs during follow-up.
- These results highlight the need for improved treatment options for this population.

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AUTHOR DISCLOSURES

This study was supported by Vertex Pharmaceuticals Incorporated. CZ, NL, and SJ are employees at Vertex Pharmaceuticals and may hold stock or stock options in the company.

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