

# Healthcare Resource Utilization Among Patients With Sickle Cell Disease With Recurrent Vaso-Occlusive Crises in Canada

Lauren Lilly<sup>1</sup>; **Chuka Udeze**<sup>1</sup>; Natalie Nightingale<sup>2</sup>; Irene Wang<sup>2</sup>; Jillian Murray<sup>2</sup>; Carlos Penaranda<sup>1</sup>; Calum Neish<sup>2</sup>; Nanxin Li<sup>1</sup>; Kevin H.M. Kuo<sup>3</sup>

<sup>1</sup>Vertex Pharmaceuticals Incorporated, Boston, MA, USA; <sup>2</sup>IQVIA Solutions Canada Inc, Ontario, CA; <sup>3</sup>University of Toronto, Toronto, Ontario, CA

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## BACKGROUND

- Sickle cell disease (SCD) is a rare genetic disorder characterized by expression of abnormal sickle hemoglobin, which leads to a variety of acute and chronic complications.<sup>1-4</sup>
- Vaso-occlusive crises (VOCs), a hallmark clinical feature in patients with SCD, cause debilitating pain and can lead to additional organ complications and increased mortality.<sup>1-3,5</sup>
- A recent study of the broad population of people with SCD conducted in Ontario, Canada found a substantial yet highly variable need for hospital-based care.<sup>6</sup>
- However, the healthcare resource utilization (HCRU) of people with SCD with recurrent VOCs in the Canadian healthcare system is not well understood.

## OBJECTIVE

- To describe the HCRU of patients with SCD with recurrent VOCs in Ontario, Canada

## METHODS

### Study Design and Database

- This longitudinal, retrospective cohort study utilized administrative datasets from the Institute for Clinical Evaluative Sciences (ICES) in Ontario, Canada to identify patients with SCD.
- The ICES database stores data collected through the routine administration of Ontario’s publicly funded healthcare and includes all publicly insured healthcare touchpoints for ~13 million people (~40% of Canadian population).
  - Physician claims, publicly reimbursed prescription claims, discharge summaries of hospital stays and emergency department visits, and claims for home care and long-term care are included in the ICES database.
  - Privately reimbursed prescription claims are not captured in the ICES database.
- The study was conducted from January 1, 2009, to December 31, 2022, and included a 12-year patient selection period (from January 1, 2010, to December 31, 2021), and a minimum of 1 year of data availability before and after study inclusion.

### Patient Identification

- Patients were included in the analysis if they met the following inclusion criteria:
  - At least one diagnosis of SCD between January 1, 2010, and December 31, 2021
  - At least two VOCs per year in at least two consecutive years in the selection period
    - VOCs were defined as SCD with crisis, priapism, or acute chest syndrome
  - At least 12 months of data availability before and after the index date (date of the second VOC in the second consecutive year)
- Patients were excluded if they met the following exclusion criteria:
  - Evidence of hematopoietic stem cell transplant (HSCT) or hereditary persistence of fetal hemoglobin prior to the index date
- All patients were followed for at least 12 months from index date to a censoring event or end of the study period (December 31, 2022)
  - A censoring event was defined as death, loss to follow-up, most recent data availability, or receipt of HSCT.

### Matched Controls

- Each patient with SCD with recurrent VOCs was exact matched without replacement to 3 non-SCD controls in the general Ontario population from ICES datasets
- Matching was based on following demographic characteristics: age (in years) at index date, sex, and Local Health Integration Networks (LHIN) of residence at index date
- Matched controls were assigned the same index date as their matched case
- Matched controls were required to have at least 12 months of data availability before and after their index date
- Matched controls were followed for at least 12 months from index date to a censoring event or end of the study period (December 31, 2022)
  - A censoring event was defined as death, loss to follow-up, most recent data availability, or receipt of HSCT

### Study Measures and Analysis

- Descriptive analyses were conducted for patient demographics and HCRU for patients with SCD with recurrent VOCs and matched controls
  - Mean (standard deviation [SD]) values were reported for continuous variables and frequencies/proportions (n,%) for categorical variables
  - All values with a count of less than 6 patients were suppressed to a range (e.g., 1-5\*), along with the second smallest group to prevent back-calculation.
- Demographics including age, sex, and income quintile were assessed at the index date
- Rate of HCRU (per patient per year [PPPY]) was calculated over the variable length follow-up period
- Rate of VOCs (PPPY) was calculated over the variable-length follow-up period
- Comparative analyses were conducted for HCRU between patients and matched controls using t-test with 2-sided alpha.  $P<0.05$  was considered statistically significant.

### Subgroup Analyses

- Two subgroup analyses were conducted for HCRU: age at index date and number of VOCs PPPY in the follow-up period
  - Age at Index date: 0 – 11 years, 12 – 35 years , and ≥36 years
  - Number of VOCs in follow-up period: <2 PPPY and ≥2 PPPY
    - Patients with ≥2 VOC/yr in the follow-up period were further broken down to 2 – <4, 4 - <10, ≥10 VOCs/year

## RESULTS

### Patient Demographics

- A total of 859 patients with SCD with recurrent VOCs were identified in ICES database and matched to 2577 controls (**Figure 1**).
- The mean age of patients with SCD was 22.1 years (SD: 14.4) and 50.9% of patients were female (**Table 1**).
- Demographics between patients with SCD and matched controls were broadly similar (**Table 1**)
- A higher proportion of patients with SCD were in the lowest income quintile compared to matched controls (38.4% vs 21.0%) (**Table 1**).

Figure 1. Attrition Table

SCD with recurrent VOCs
≥1 SCD diagnosis code(s) in ED/inpatient abstract between January 1, 2010 and December 31, 2021 N = 3801
≥2 VOC claims <sup>a</sup> per year during any 2 consecutive years in the selection period N = 886
†
Included patients <sup>b</sup> N = 859

HSCT: hematopoietic stem cell transplant; HPHH: hereditary persistence of fetal hemoglobin; ICES: Institute for Clinical Evaluative Sciences; OHIP: Ontario health insurance plan; SCD: sickle cell disease; VOCs: vaso-occlusive crises  
\*VOCs defined as having ICD-10-CA diagnosis codes for any of the following conditions: sickle cell anemia with crisis, priapism, or acute chest syndrome.  
†Additional exclusion criteria include <12 months data availability before and after index date, age >100 years at index date, non-Ontario resident at index date, invalid OHIP card number, presence of a HSCT at any time before index date, diagnosis of HPHH between April 1, 2002, and index date; and missing date of birth, sex, or postal code

Table 1. Baseline Demographics		
	SCD w/recurrent VOCs N = 859	Matched controls N = 2577
Sex, n (%)		
Female	437 (50.87)	1311 (50.87)
Male	422 (49.13)	1266 (49.13)
Age at index date, years		
Mean ± SD, min-max	22.07 ± 14.41, 1-85	22.08 ± 14.44, 1-86
Age categories, n (%), years		
0-11	220 (25.61)	655 (25.42)
12-35	499 (58.09)	1510 (58.6)
≥36	140 (16.3)	412 (15.99)
New Ontario resident, n (%)		
Yes	133 (15.48)	175 (6.79)
Income quintile, n (%) <sup>a,b</sup>		
1 (Lowest)	330 (38.42)	542 (21.03)
2	200 (23.28)	488 (18.94)
3	182 (21.19)	580 (22.51)
4	104 (12.11)	501 (19.44)
5 (Highest)	40 (4.66)	463 (17.97)
Years of follow-up, mean (SD)	7.44 (3.20)	7.66 (3.14)

\*3 patients from each group had missing data  
†Income quintiles were calculated at the neighborhood level (with each containing 400 to 700 people) using census data, with the first quintile having the lowest median income and the fifth quintile having the highest median income

Table 2. HCRU		
	SCD w/recurrent VOCs N = 859	Matched controls N = 2577
Emergency department visits PPPY <sup>a,b</sup>		
Mean (SD)	3.03 (5.00)	0.28 (0.47)
Median (Min-Max)	1.96 (0.00 – 88.52)	0.12 (0.00 – 6.29)
Inpatient hospitalizations PPPY <sup>a,b</sup>		
Mean (SD)	1.64 (1.83)	0.04 (0.19)
Median (Min-Max)	1.05 (0.00 – 16.38)	0.00 (0.00 – 8.30)
Days in hospitals PPPY <sup>a,b</sup>		
Mean (SD)	11.67 (20.68)	0.17 (1.16)
Median (Min-Max)	5.11 (0.00 – 174.42)	0.00 (0.00 – 33.18)
Hospital outpatient clinic visits PPPY <sup>a,b</sup>		
Mean (SD)	4.11 (4.02)	0.31 (1.30)
Median (Min-Max)	2.98 (0.00 – 38.91)	0.00 (0.00 – 50.21)
Outpatient general practitioner visits PPPY <sup>a,b</sup>		
Mean (SD)	3.60 (4.80)	2.62 (2.99)
Median (Min-Max)	2.21 (0.00 – 56.01)	1.76 (0.00 – 37.10)
Outpatient specialist visits PPPY <sup>a,b</sup>		
Mean (SD)	6.28 (5.03)	1.21 (2.32)
Median (Min-Max)	4.94 (0.00 – 41.72)	0.46 (0.00 – 62.43)
Outpatient Prescriptions PPPY <sup>a,b,c</sup>		
Mean (SD)	19.38 (46.50)	1.98 (12.62)
Median (Min-Max)	4.70 (0.00 – 643.30)	0.20 (0.00 – 361.24)
Imaging tests PPPY <sup>a,b</sup>		
Mean (SD)	1.85 (1.71)	0.25 (0.59)
Median (Min-Max)	1.40 (0.00 – 11.86)	0.00 (0.00 – 14.84)
Laboratory tests PPPY <sup>a,b</sup>		
Mean (SD)	1.68 (1.99)	0.84 (1.25)
Median (Min-Max)	1.12 (0.00 – 21.42)	0.41 (0.00 – 21.35)

HCRU: healthcare resource utilization; PPPY: per person per year; SD: standard deviation; VOCs: vaso-occlusive crises.  
\* $P<0.001$   
†Rate PPPY of healthcare resource use was calculated at the patient level; summary statistics were calculated across all patients in the cohort  
‡ $N = 177$  patients with SCD and  $N = 1659$  matched controls with at least one outpatient prescription claim

### HCRU

- Patients with SCD with recurrent VOCs experienced an average of 3.2 VOCs PPPY during the follow-up period
- Patients had a mean of 1.6 inpatient hospitalizations, 11.7 days spent in the hospital, and 3.0 emergency department visits (all PPPY) (**Table 2**)
- Patients with SCD with recurrent VOCs had significantly ( $P<0.05$ ) higher HCRU compared to matched controls (**Table 2**)

### Subgroup Analysis: HCRU

- HCRU increased as patient age increased
  - Patients in the oldest age cohort (i.e., ≥ 36 years) had the highest mean rates of ED visits (3.5 PPPY) and days spent in the hospital (15.8 PPPY) (**Table 3**)
- Patients with a higher number of VOCs (≥2 VOCs PPPY in the follow-up period) had higher HCRU than those with a lower number of VOCs (<2 VOCs PPPY in the follow-up period) (**Table 4**)
- As number of VOCs increased, HCRU increased as well (**Table 4**)

Table 3. HCRU Subgroups by Age			
	0-11 years n = 220	12-35 years n = 499	≥36 years n = 140
Emergency department visits PPPY <sup>a</sup>			
Mean (SD)	1.98 (1.50)	3.37 (4.75)	3.49 (8.24)
Median (Min-Max)	1.65 (0.00 – 8.38)	2.11 (0.00 – 63.47)	1.95 (0.00 – 88.52)
Inpatient hospitalizations PPPY <sup>a</sup>			
Mean (SD)	1.24 (1.09)	1.83 (2.06)	1.57 (1.81)
Median (Min-Max)	0.95 (0.09 – 7.54)	1.15 (0.00 – 16.38)	0.95 (0.00 – 10.52)
Days in hospitals PPPY <sup>a</sup>			
Mean (SD)	6.18 (9.47)	12.93 (21.76)	15.83 (27.04)
Median (Min-Max)	3.81 (0.18 – 97.25)	5.96 (0.00 – 159.87)	5.07 (0.00 – 174.42)
Hospital outpatient clinic visits PPPY <sup>a</sup>			
Mean (SD)	3.34 (2.36)	4.27 (4.07)	4.77 (5.49)
Median (Min-Max)	2.81 (0.00 – 19.05)	3.05 (0.00 – 25.09)	3.44 (0.00 – 38.91)
Outpatient general practitioner visits PPPY <sup>a</sup>			
Mean (SD)	1.29 (1.39)	3.80 (4.42)	6.51 (7.21)
Median (Min-Max)	0.88 (0.00 – 8.89)	2.70 (0.00 – 48.38)	4.27 (0.00 – 56.01)
Outpatient specialist visits PPPY <sup>a</sup>			
Mean (SD)	5.10 (3.22)	6.30 (5.04)	8.07 (6.61)
Median (Min-Max)	4.50 (0.00 – 19.98)	4.77 (0.00 – 33.71)	6.91 (0.00 – 41.72)
Outpatient Prescriptions PPPY <sup>a,b</sup>			
Mean (SD)	9.49 (11.35)	18.68 (48.22)	37.42 (65.78)
Median (Min-Max)	5.49 (0.00 – 86.28)	3.88 (0.00 – 643.30)	5.71 (0.00 – 362.62)
Imaging tests PPPY <sup>a</sup>			
Mean (SD)	1.47 (0.92)	1.87 (1.78)	2.36 (2.22)
Median (Min-Max)	1.41 (0.00 – 5.69)	1.33 (0.00 – 11.45)	1.70 (0.00 – 11.86)
Laboratory tests PPPY <sup>a</sup>			
Mean (SD)	1.45 (1.76)	1.54 (1.68)	2.52 (2.91)
Median (Min-Max)	0.77 (0.00 – 9.25)	1.11 (0.00 – 16.05)	1.83 (0.00 – 21.42)

SD: standard deviation; PPPY: per person per year; HCRU: healthcare resource utilization  
†Rate PPPY of healthcare resource use was calculated at the patient level; summary statistics were calculated across all patients in the cohort; ‡ $n = 777$  patients with SCD and  $n = 1659$  matched controls with at least one outpatient prescription claim

Table 4. HCRU by Number of VOCs					
	<2 VOCs per year n = 454	≥2 VOCs per year n = 405	2 to <4 VOCs per year n = 215	4 to <10 VOCs per year n = 145	≥10 VOCs per year n = 45
Emergency department visits PPPY <sup>1a</sup>					
Mean (SD)	1.29 (0.92)	4.98 (6.71)	2.63 (1.51)	5.09 (2.93)	15.88 (15.02)
Median (Min-Max)	1.11 (0.00 – 5.95)	3.13 (0.61 – 88.52)	2.39 (0.61 – 19.74)	4.86 (0.78 – 30.02)	10.38 (5.03 – 88.52)
Inpatient hospitalizations PPPY <sup>a</sup>					
Mean (SD)	0.67 (0.40)	2.72 (2.17)	1.57 (0.62)	3.08 (1.17)	7.07 (3.28)
Median (Min-Max)	0.63 (0.00 – 3.09)	2.02 (0.00 – 16.38)	1.54 (0.00 – 5.12)	2.90 (0.00 – 7.51)	6.53 (1.50 – 16.38)
Days in hospitals PPPY <sup>a</sup>					
Mean (SD)	3.52 (3.63)	20.81 (27.11)	9.79 (9.72)	25.68 (28.06)	57.79 (40.53)
Median (Min-Max)	2.67 (0.00 – 33.36)	11.05 (0.00 – 174.42)	7.34 (0.00 – 80.73)	16.59 (0.00 – 159.87)	41.83 (3.63 – 174.42)
Hospital outpatient clinic visits PPPY <sup>a</sup>					
Mean (SD)	3.23 (3.16)	5.10 (4.62)	3.74 (3.25)	6.03 (5.53)	8.56 (4.53)
Median (Min-Max)	2.47 (0.00 – 25.09)	3.83 (0.00 – 38.91)	3.02 (0.00 – 23.76)	4.68 (0.00 – 38.91)	8.25 (0.73 – 23.14)
Outpatient general practitioner visits PPPY <sup>a</sup>					
Mean (SD)	3.10 (3.55)	4.16 (5.84)	3.68 (5.21)	4.92 (7.05)	3.96 (4.00)
Median (Min-Max)	1.96 (0.00 – 27.24)	2.56 (0.00 – 56.01)	2.42 (0.00 – 56.01)	2.79 (0.00 – 48.38)	2.51 (0.00 – 20.35)
Outpatient specialist visits PPPY <sup>a</sup>					
Mean (SD)	5.28 (4.27)	7.40 (5.57)	6.02 (4.41)	8.34 (6.49)	11.00 (5.15)
Median (Min-Max)	4.19 (0.00 – 32.72)	5.95 (0.00 – 41.72)	4.91 (0.00 – 36.61)	6.93 (0.00 – 41.72)	10.43 (1.66 – 27.16)
Outpatient Prescriptions PPPY <sup>a,b</sup>					
Mean (SD)	10.66 (28.32)	29.15 (59.26)	15.19 (31.75)	35.49 (59.81)	75.44 (111.15)
Median (Min-Max)	2.80 (0.00 – 416.24)	7.72 (0.00 – 643.30)	5.02 (0.00 – 329.47)	10.53 (0.00 – 362.62)	37.53 (0.00 – 643.30)
Imaging tests PPPY <sup>a</sup>					
Mean (SD)	1.23 (0.94)	2.54 (2.08)	1.77 (1.17)	3.01 (2.23)	4.72 (2.93)
Median (Min-Max)	1.05 (0.00 – 5.21)	1.91 (0.00 – 11.86)	1.54 (0.00 – 7.19)	2.34 (0.00 – 11.86)	4.85 (0.29 – 11.45)
Laboratory tests PPPY <sup>a</sup>					
Mean (SD)	1.76 (2.19)	1.59 (1.72)	1.76 (1.80)	1.48 (1.69)	1.11 (1.34)
Median (Min-Max)	1.16 (0.00 – 21.42)	1.087 (0.00 – 14.30)	1.12 (0.00 – 13.13)	1.15 (0.00 – 14.30)	0.63 (0.00 – 6.52)

HCRU: health care resource utilization; SD: standard deviation; PPPY: per person per year; VOCs: vaso-occlusive crises.  
†Rate PPPY of healthcare resource use was calculated at the patient level; summary statistics were calculated across all patients in the cohort; ‡ $n = 777$  patients with SCD and  $n = 1659$  matched controls with at least one outpatient prescription claim.

## LIMITATIONS

- The data collected in this study are based on provincial medical records. Therefore, correct identification of individuals clinically managed for SCD using diagnosis codes is limited by accuracy of billing code in inpatient encounters.
- Prescription drug data was only available through the public payer and does not capture drugs paid for by private insurance or the consumer. As a result, drug claims by adults aged 25 to 64 with no disability or financial need were underrepresented in this database.
- Given the minimum 12-month post-index period for patients with SCD, individuals who died, or were not continuously enrolled for at least 12 months post-index date were excluded, which potentially could lead to underestimation of HCRU.
- VOCs may not be adequately captured in administrative databases in Ontario due to patients managing them at home, which could lead to underestimation of rate of VOCs in this patient population.

## CONCLUSIONS

- Patients with SCD with recurrent VOCs had significantly higher HCRU than the matched general population controls driven by ED visits and days spent in hospital in Canada.
- Older age and higher number of VOCs was associated with higher HCRU.
- Elevated HCRU in patients with SCD with recurrent VOCs highlight the need for novel therapies in this space that can reduce number of VOCs and the associated HCRU.

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## DISCLOSURES

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