

Sustained Humanistic Burden and Work Impact in Adults With Sickle Cell Disease With Recurrent Vaso-Occlusive Crises: Results From a Global Longitudinal Survey

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INTRODUCTION

- Sickle cell disease (SCD) is characterized by vaso-occlusive crises (VOCs) and a progressive clinical course that leads to end-organ damage and reduced life expectancy¹
- Individuals living with SCD with recurrent VOCs experience disruptions to their daily lives, including debilitating chronic pain and fatigue, that affect their ability to work and substantially impair their health-related quality of life (HRQoL)²
- Practice guidelines support treating most patients with SCD with hydroxyurea, particularly those with recurrent VOCs³; however, adherence is suboptimal⁴
- Fatigue has been reported as a major concern for patients with SCD; however, the severity and impact of fatigue have been under-reported and not well quantified, especially in adults⁵
- Few studies have assessed disease impacts, such as work productivity and financial concerns, in patients with SCD; additionally, sparse longitudinal data exist
- Therefore, we aimed to evaluate HRQoL longitudinally, as well as evaluate fatigue, work productivity impairments, and financial concerns among adults with SCD with recurrent VOCs

OBJECTIVES

- To better understand the humanistic burden associated with living with SCD in individuals with recurrent VOCs receiving standard-of-care treatments, including:
 - To evaluate the impact of SCD on HRQoL and HRQoL longitudinally, using patient-reported outcome (PRO) measures
 - To measure the severity of fatigue using a PRO measure
 - To assess work productivity impacts and financial concerns

METHODS

Study Design

- An online longitudinal survey was administered at 3 timepoints (Month 0 [baseline], Month 3, and Month 6) to participants in the United States and Europe (the United Kingdom, France, Germany, and Italy)
- The results presented here focus on the findings from Month 3, including newly administered questions, and the changes in PRO measure scores since Month 0

Key Inclusion Criteria

- Self-reported SCD diagnosis
- At least 2 VOCs per year for 2 years that required an interaction with a medical facility and administration of pain medication or red blood cell transfusion (RBCT)
- Aged ≥18 years

Statistical Analysis

- Descriptive analyses were conducted for participant characteristics and PRO measures based on survey findings among those completing surveys at Month 0 and 3
- Minimal clinically important differences (MCIDs) and US general population data are provided for context, as available

Survey Design and Administration

- Questions were informed by qualitative interviews with individuals living with SCD in the United States and United Kingdom and the scientific advisory team consisting of clinicians, patient advocates, and outcomes researchers
- Month 3 survey invitations were sent to Month 0 participants, who were first informed of the study via multichannel outreach by patient advocacy groups
- The Month 3 survey included bespoke questions related to time required to manage the disease, out-of-pocket expenses, and financial concerns, including burden and distress
- PRO measures were included to assess the impact of SCD on HRQoL, fatigue, and work productivity and activity impairment (Table 1)

Table 1. Longitudinal Survey: PRO Measures

PRO Measure	Description
Functional Assessment of Cancer Therapy - Bone Marrow Transplantation (FACT-BMT)⁶	General measure of HRQoL (FACT-General [FACT-G]) and treatment-specific concerns of bone marrow transplantation section (BMT subscale; data not shown)
EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L) and Visual Analog Scale (VAS)⁷	General measure of health status and self-rated health
Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me)⁸	SCD-specific HRQoL measure of physical, social, and emotional impact
Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue)⁹	Measure of the severity and impact of fatigue, including the physical, functional, emotional, and social consequences
Pain 11-point numeric rating scale (Pain NRS)¹⁰	Common measure of pain intensity ranging from 0 (no pain) to 10 (worst pain imaginable)
Work Productivity and Activity Impairment (WPAI)¹¹	Quantifies impairments in paid work and unpaid activity due to a condition

HRQoL, health-related quality of life; PRO, patient-reported outcome.

RESULTS

Demographics

- The Month 0 and 3 surveys were completed by 118 adults with SCD with recurrent VOCs living in the United States (n = 73) and Europe (United Kingdom, Germany, Italy, and France; n = 45) (Table 2)
- Overall, 72.9% of participants were female, with a mean age of 34.7 years (standard deviation [SD]: 10.2) (Table 2)
- Only 16.9% of participants had full-time employment (≥32 hours/week), and 61.0% of participants were unemployed or unable to work due to SCD (Table 2)

Table 2. Baseline Demographics

	Adults With SCD With Recurrent VOCs (N = 118)
Age (years), mean (SD)	34.7 (10.2)
Geography, n (%)	
United States	73 (61.9)
Europe (United Kingdom, Germany, Italy, and France)	45 (38.1)
Gender, n (%)	
Female	86 (72.9)
Male	31 (26.3)
Non-binary	1 (0.8)
Employment, n (%)	
Unemployed	40 (33.9)
Unable to work or on leave due to SCD	32 (27.1)
Part-time (<32 hours/week)	21 (17.8)
Full-time (≥32 hours/week)	20 (16.9)
Retired	4 (3.4)
Unpaid volunteer	3 (2.5)

SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

Reporting data for participants who completed both Month 0 and 3 surveys.

Clinical Characteristics

- In each of the past 2 years, participants reported a mean of 6 severe VOCs (Table 3)
- In the past 3 months, patients experienced a mean of 1.4 hospital visits with overnight stays due to VOCs and 5.4 total overnight days hospitalized (Table 3)

Table 3. Clinical Characteristics

	Adults With SCD With Recurrent VOCs (N = 118)
Annual severe VOCs,^a mean (SD)	
Past year (2021–2022)	6.0 (4.9)
Prior year (2020–2021)	5.9 (4.6)
Hospital visits in the past 3 months due to VOCs, mean (SD)	
Accident and emergency/emergency room visits	2.2 (2.9)
Hospital visits with overnight stay	1.4 (2.0)
Total overnight days hospitalized	5.4 (7.5)

RBCT, red blood cell transfusion; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

^aDefined as requiring an interaction with a medical facility and administration of pain medication or a RBCT.

Current Treatments

- In the past month, 59.3% of participants reported being prescribed and taking hydroxyurea (Table 4)
- The 2 most cited reasons for not taking hydroxyurea included “healthcare provider has not prescribed it” (33.3%) and “I do not like side effects/I can’t tolerate it” (29.2%) (data not shown)

Table 4. Treatments in the Past Month

Current Treatment in Past Month, n (%)	Adults With SCD With Recurrent VOCs at Month 3 (N = 118)
Hydroxyurea	70 (59.3)
Prescription pain medication	88 (74.6)
Over-the-counter pain medication	50 (42.4)
RBCTs	
Exchange transfusions	19 (16.1)
Regular/top-up infusions	17 (14.4)
Crizanlizumab	9 (7.6)
Voxelotor	9 (7.6)
L-glutamine	10 (8.5)

RBCT, red blood cell transfusion; SCD, sickle cell disease; VOC, vaso-occlusive crisis.

FACT-G: Month 3

- Participants reported lower HRQoL on the FACT-G (total score) at Month 3 (59.8) compared with the US general population (80.1), and each domain score was lower than that of the US general population¹² (Table 5)
- The FACT-G total score changed by an average of −3.2 points from Month 0 to 3, reaching the lower threshold of the MCID range of 3 to 7 points. This PRO measure suggests that, on average, HRQoL impacts were consistent over time with minor worsening (Figure 1A)

Table 5. FACT-G Results

FACT-G Domain, Mean Score (SD)	Score Range ^a	Adults With SCD With Recurrent VOCs at Month 3 (N = 118)	US General Population ¹²
Physical wellbeing	0–28	14.1 (6.5)	22.7 (5.4)
Social and family wellbeing	0–28	16.7 (7.0)	19.1 (6.8)
Emotional wellbeing	0–24	14.4 (5.6)	19.9 (4.8)
Functional wellbeing	0–28	14.6 (6.5)	18.5 (6.8)
Total score	0–108	59.8 (19.6)	80.1 (18.1)

FACT-G, Functional Assessment of Cancer Therapy – General; HRQoL, health-related quality of life; MCID, minimal clinically important difference; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

^aHigher scores indicate better HRQoL. FACT-G MCID range is 3 to 7 points (based on publications in other hematological conditions).^{12,13}

EQ-5D-5L: Month 3

- Participants reported substantially lower mean health utility scores on the EQ-5D-5L at Month 3 (0.55) compared with the US general population (0.85)¹⁵ (Table 6)

Table 6. EQ-5D-5L Results

EQ-5D-5L utility score, mean (SD)	Score Range ^a	Adults With SCD With Recurrent VOCs at Month 3 (N = 118)	US General Population ¹⁵
EQ-5D-5L utility score, mean (SD)	0 (dead) – 1 (full health)	0.55 (0.28)	0.85 (0.21)

EQ-5D-5L, EuroQoL 5 Dimensions 5 Levels; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

^aSome health states produce negative health utility scores (worse than death).¹⁵

- Average utility scores from Month 0 to 3 remained nearly unchanged among participants with SCD (−0.04 points), suggesting that, on average, their reduced health utility was consistent over time while they were receiving standard-of-care treatments (Figure 1B)

ASCQ-Me: Month 3

- Compared with a large population of US adults with SCD (mean 50 across all domains),⁸ participants with SCD with recurrent VOCs, on average, reported substantially greater pain impact (45.3) and stiffness impact (45.3) and slightly greater emotional impact (45.5) and social functioning impact (45.5) (lower scores represent higher impact/worse functioning) (Table 7)
- Average scores from Month 0 to 3 across all domains changed by −0.5 to 4.5 points, suggesting that SCD-specific HRQoL impacts were sustained while participants received standard-of-care treatments (Figure 1C)

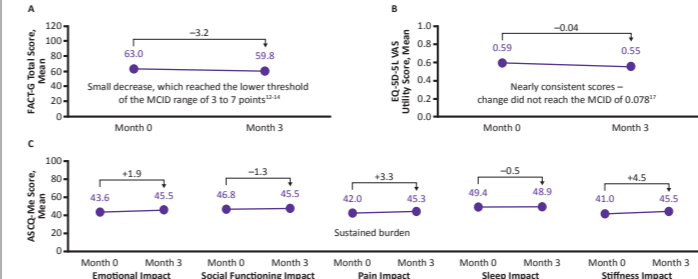
Table 7. ASCQ-Me Results

ASCQ-Me Domain, Mean Score (SD)	Adults With SCD With Recurrent VOCs at Month 3 (N = 118)
Emotional impact	45.5 (7.7)
Social functioning impact	45.5 (7.7)
Pain impact	45.3 (9.4)
Sleep impact	48.9 (6.1)
Stiffness impact	45.5 (8.0)

ASCQ-Me, Adult Sickle Cell Quality of Life Measurement Information System; MCID, minimal clinically important difference; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

Higher scores indicate better functioning. A score of 50 is the average among a large population of US adults with SCD.⁸

Figure 1. Sustained HRQoL Impact of TDT Over Time as Measured by A) FACT-G, B) EQ-5D-5L Health Utility, and C) ASCQ-Me



ASCQ-Me, Adult Sickle Cell Quality of Life Measurement Information System; EQ-5D-5L, EuroQoL 5 Dimensions 5 Levels; FACT-G, Functional Assessment of Cancer Therapy – General; HRQoL, health-related quality of life; MCID, minimal clinically important difference; SCD, sickle cell disease; SD, standard deviation; VAS, Visual Analog Scale; VOC, vaso-occlusive crisis.

FACIT-Fatigue: Month 3

- The average fatigue score for participants with SCD with recurrent VOCs was 24.2, which is substantially lower than the US general population average (43.6)^{13,18} (Table 8)
- On average, the average fatigue score of participants with SCD with recurrent VOCs (24.2) was comparable to that of patients with anemia and cancer (23.9)¹²
- Among participants, 63.1% felt fatigued quite a bit or very much of the time in the past 7 days (item-level response; data not shown)

Table 8. FACIT-Fatigue Subscale Results

	Score Range	Adults With SCD With Recurrent VOCs at Month 3 (N = 103) ^b	US General Population ^{12,14}	Patients With Anemia and Cancer ¹²
FACIT-Fatigue score, mean (SD)^{a,b}	0–52 ^{13,18}	24.2 (10.2)	43.6 (9.4)	23.9 (12.6)

FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy – Fatigue; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

^aNumber of survey responses: 103; ^bLower numbers indicate higher fatigue.¹³

Pain 11-Point NRS: Month 3

- The average current pain score reported on the Pain NRS was 4.5 (SD: 2.4), which is commonly categorized as moderate pain severity¹⁹
- The average current pain reported on the Month 0 survey was about 10% lower than reported on the Month 3 survey (4.1 [SD: 2.6])

WPAI: Month 3

- Employed participants missed an average of 12.6 hours of work in the past week due to SCD, corresponding to an average absenteeism of 31.9% (Table 9)
- Overall, work productivity in the past week was reduced by 63.7%
- Among participants, 97.5% reported daily activity impairment (data not shown) and overall, there was a 59.3% mean reduction in daily activities in the past week

Table 9. WPAI Results

WPAI Domain	Mean (SD)
Absenteeism: Work time missed, %^a	31.9 (32.6)
Presenteeism: Reduced effectiveness/impairment, %^a	44.8 (29.0)
Work productivity loss: Overall work impairment, %^a	63.7 (28.1)
Activity impairment, %^b	59.3 (24.0)
Work missed in the last 7 days, hours^a	12.6 (16.1)

SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis; WPAI, Work Productivity and Activity Impairment.

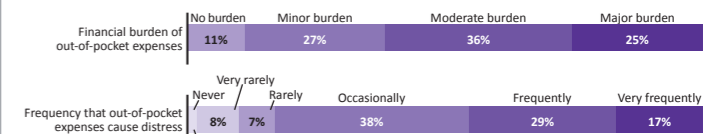
Higher WPAI percentages represent increased impairment.

^an = 48 (participants indicating employment on WPAI); ^bn = 118.

Financial Burden and Distress: Month 3

- Among participants with SCD with recurrent VOCs, 58.5% reported that they did not have sufficient money to cover the costs associated with managing their condition and estimated that they would need an additional median of \$300 per month (interquartile range: \$200–\$650)
- Out-of-pocket expenses were reported to be a moderate-to-major burden for 61.9% of participants (Figure 2)
- Financial distress was reported to be experienced frequently or very frequently by 46% of participants (Figure 2)

Figure 2. Financial Burden and Distress



LIMITATIONS

- Study participants were self-selected and needed access to the Internet and email, which may impact the generalizability of these results
- All data were self-reported; eligibility and clinical data were not directly verified by a clinician

CONCLUSIONS

- Despite receiving current treatments, adults with SCD with recurrent VOCs experienced significant and sustained negative impacts on HRQoL, as measured by the FACT-G, EQ-5D-5L, ASCQ-Me, Pain NRS, and WPAI
- Participants with SCD with recurrent VOCs reported severe fatigue, with scores similar to patient with anemia and cancer, as measured by the FACIT-Fatigue
- Most participants (58.5%) reported that they had insufficient money to cover the costs associated with managing SCD and that most of their out-of-pocket expenses were a moderate-to-major burden, and nearly half of participants reported that they frequently or very frequently experienced financial distress
- Taken together, these results demonstrate the substantial humanistic burden among those living with SCD with recurrent VOCs and the significant unmet needs in this patient population

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