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Poster xxxx

An international, longitudinal, observational study to evaluate the psychometric properties of a daily diary for adolescents and adults with sickle cell disease

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KEY FINDINGS & CONCLUSIONS

- **Primary Conclusion**: The SCPD-S Daily VOC Impact score, comprised of items 11-16, is a reliable and valid measure of VOC impact, and is suitable for use in trials, observational studies, and clinic settings
- The SCPD-S evaluates VOC frequency and duration, experiences during a VOC (e.g., medication use, healthcare visits), and provides a daily measure of VOC impact
- Compliance with completing the daily diary was 87%
- The SCPD-S Daily VOC Impact Scale 1 (items 11-16) showed sufficient evidence of reliability and validity across psychometric properties. Scale 2 had weaker evidence, particularly in its ability to detect change
  - Scale 1 should be used as a measure of daily VOC impact
  - Scale 2 should be dropped from the diary
- Limitations: difficulty identifying stable patients for evaluation of test-retest reliability due to the inherent variability in VOCs, use of a convenience sample, and data collection during the COVID-19 pandemic, which could impact experiences during a VOC
- Strengths: use of a study design that supports the feasibility of the daily diary in patients across ages and geographic regions, and use of development and validation procedures that followed best practice guidelines

INTRODUCTION

- Vaso-occlusive crises (VOCs) are caused by multi-cell adhesion or cell clusters that block or reduce blood flow, and are one of the most serious complications of sickle cell disease (SCD)[1-3]
- Because VOCs occur sporadically and unpredictably, a daily diary – the Sickle Cell Pain Diary - Self Report (SCPD-S) – was developed to more accurately capture the frequency, duration, severity of pain, and related impacts experienced during a VOC, including VOCs managed at home (**Figure 1**)[4]
  - Each day, respondents indicate if they have experienced a VOC (referred to as a "sickle cell pain crisis") in the past 24 hours
  - If they have not experienced a VOC, respondents answer 5 questions on the impact of SCD over the past 24 hours
  - If they have experienced a VOC, respondents answer 19 questions about the VOC over the past 24 hours

OBJECTIVE

To evaluate the measurement model, scoring, and psychometric properties of the SCPD-S VOC impact through data collected from an international, longitudinal, observational study

METHODS

Participant eligibility:
- Confirmed diagnosis of SCD
- Age 12 or older
- Currently live in the United States (US), United Kingdom (UK), or Kingdom of Saudi Arabia (KSA)
- Experienced ≥1 VOC in the past 12 months

Participants were recruited through participant panels, advocacy groups, and clinician referrals

Study Design:
- The survey was administered through a mobile application downloaded onto patients' devices
- Patients completed survey questions every day for at least 3 months
  - The SCPD-S was administered every day
  - Other assessments were administered at pre-specified intervals, which served as criterion variables for planned analyses (**Figure 2**)
- Patients could backfill up to 2 days of missed surveys
- The analytic sample included patients who experienced at least 1 VOC while enrolled in the study and who completed ≥25 of 30 daily assessments during the month the VOC occurred

Measurement Model:
- Multi-level factor analyses were conducted in a nested setting, where daily assessments were nested within each individual patient (within- and between-patient levels)
- The hypothesized unidimensional model of VOC impact was tested with a confirmatory factor analysis (CFA); split-half exploratory factor analyses (EFAs) and follow-up CFAs were conducted to explore alternative/refined models
  - Acceptable model fit: confirmatory fit index (CFI) ≥0.90; root mean square error of approximation (RMSEA) ≤0.08; standardized root mean square residual (SRMR) ≤0.08
- Cronbach's alpha evaluated internal consistency reliability
  - Acceptable Cronbach's alpha: 0.70

Item-Level Properties:
- Analyses of item-level data, including evaluation of item/floor effects, Mokken scale analyses, and inter-item correlations were conducted on VOC impact items. Results were satisfactory and are not presented here

Differential Item Functioning (DIF):
- Analyses examined whether different groups of patients respond differently to VOC impact items, even after controlling for levels of the underlying latent trait
- DIF due to age and country of residence was examined using a series of ordinal logistic regression models

SCPD-S Scoring:
- Three different SCPD-S VOC impact scores were investigated:
  - SCPD-S Daily VOC Impact Score: the overall impact of the VOC on a given day. One score is produced for each day a VOC is experienced
  - SCPD-S 7-Day VOC Impact Aggregate: the average of daily scores over a 7-day period
  - VOC Experience Impact Aggregate: the average of daily scores over days on which a VOC was experienced
- All scores range from 0-100; higher scores indicate more impact
- This poster focuses on psychometric analyses of the Daily VOC Impact Score

Psychometric Analyses:
- **Test-Retest Reliability:** Intraclass correlation coefficients (ICC) evaluated agreement between scores at different time points among a subset of stable patients defined by responses on the Patient Global Impression of Severity (PGI-S) item
  - Moderate ICC: ≥0.50; Good ICC: ≥0.75
- **Convergent Validity:** Pearson correlations were conducted between VOC impact scores and criterion variables
  - Acceptable convergent validity: ≥0.30
- **Known-Groups Validity:** VOC impact scores were compared across groups of patients who differ according to pre-defined criteria
  - Acceptability interpreted through patterns of means, effect sizes (ES), and p-values
  - ES interpretation: Negligible: 0.2< |ES|; Small: 0.2≤ |ES| <0.5; Medium: 0.5≤ |ES| <0.8; Large: |ES| ≥0.8
- **Responsiveness:** Change in VOC impact scores were correlated with change in criterion variables. Mean change in VOC impact scores were also examined as a function of change in symptom severity
  - Acceptable correlations: ≥0.30; mean change: interpreted through patterns of means, ES, and p-values

Figure 1. SCPD-S Item Content

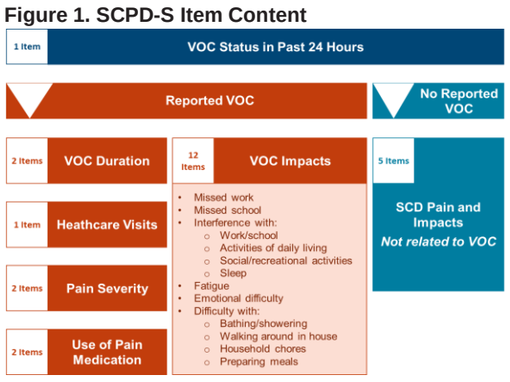
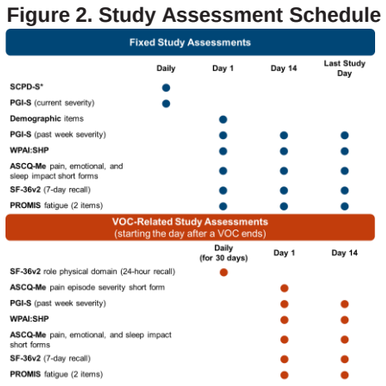


Figure 2. Study Assessment Schedule



RESULTS

Patient Sample

- The analytic sample included 299 patients (**Figure 3**)
- Demographic characteristics of the analytic sample and experiences while enrolled in the study are presented in **Table 1**

Figure 3. Overview of Patient Disposition

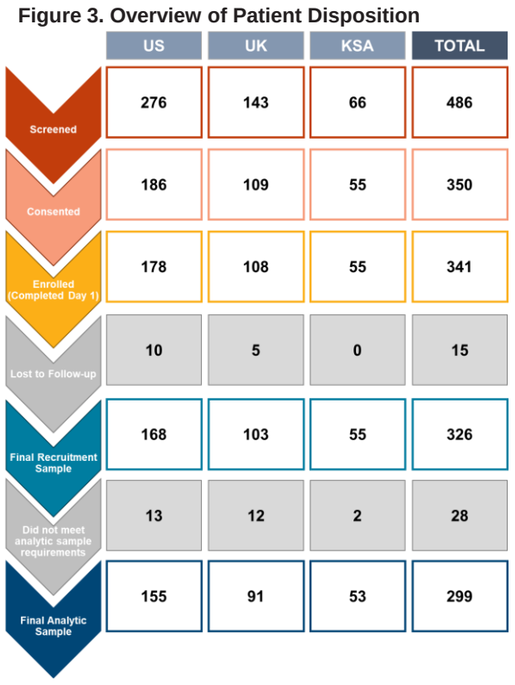


Table 1. Patient Characteristics

Demographics	Mean (SD) / N (%)
Age, years	30.3 (10.24)
Gender, female	215 (72%)
Race, Black or African	246 (83%)
Employment Status	
Student	79 (27%)
Employed (full or part time)	85 (29%)
Disabled/unable to work	64 (22%)
Unemployed	42 (14%)
Other	28 (9%)
SCD Type	
Hb-SS	159 (53%)
Hb-SC	55 (19%)
Hb-S beta thalassemia (+ or 0)	29 (10%)
Hb-SD	1 (0.3%)
Hb-SO	1 (0.3%)
Not known	53 (18%)
Experiences in the study	**Mean (SD)**
Number of VOCs experienced	6.8 (5.35)
Duration of first VOC, days	7.0 (19.19)
Duration of study enrollment, days	100.8 (18.65)

Of the 299 patients in the study, 1 patient is missing demographic information.

Measurement Model

Factor Analyses

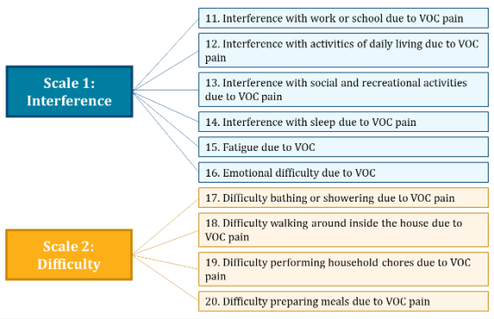
- The unidimensional model with constrained factor loadings yielded poor fit (**Table 2, Model 1**); a model with unconstrained factor loadings showed nearly identical results (data not shown)
- Two EFAs examined model fit for a 2-factor (**Table 2, Model 2**) and 3-factor solution (data not shown)
  - The 2-factor solution was selected, as it was the simplest model with good fit
- A 2-factor CFA with constrained factor loadings was conducted (**Table 2, Model 3**)
  - Refinements to the model were considered, allowing for unconstrained factor loadings and for a single item to cross-load onto both factors (data not shown)
  - The model with constrained factor loadings across levels was retained as the final model for parsimony (i.e., Model 3). Item content for each factor is shown in **Figure 4**
- A bi-factor model indicated that the measurement model is not suited to a single general factor (data not shown)

Table 2. Model Fit Statistics

Fit Statistics	Model 1	Model 2	Model 3
χ^2	2034.57 (df=79)	307.18 (df=52)	286.45 (df=76)
CFI	0.78	0.95	0.95
RMSEA	0.11	0.07	0.06
SRMR			
Within	0.10	0.04	0.03
Between	0.10	0.05	0.07

Model 1: Unidimensional CFA; Model 2: 2-Factor EFA; Model 3: 2-Factor CFA with constrained factor loadings (final model).

Figure 4. Two-Factor Model of SCPD-S VOC Impact



Internal Consistency Reliability

- Internal Consistency Reliability of the two factors was acceptable
  - Factor 1, Cronbach's alpha = 0.87
  - Factor 2, Cronbach's alpha = 0.86

Differential Item Functioning

- Neither age nor country of residence substantially increased the amount of explained variance in item responses to the SCPD-S
- Results show that when conditioning on the latent trait, respondents of different ages and different countries of residence endorse SCPD-S VOC impact items in a similar manner
- DIF due to age and country of residence is not a concern for Scale 1 or Scale 2 SCPD-S items

Psychometric Properties of the SCPD-S Daily VOC Impact Score

Test-Retest Reliability

- Test-retest reliability was good for Scale 1 (N = 114, ICC = 0.78 [95% confidence interval = 0.71-0.86]) and moderate for Scale 2 (N = 114, ICC = 0.66 [95% confidence interval = 0.56-0.76])

Convergent Validity

- Both scales were correlated with VOC pain severity at its worst and at its least (**Table 3**)
- Scale 1 showed slightly stronger relationships with pain severity than Scale 2

Known-Groups Validity

- Patients with greater symptom severity had significantly higher SCPD-S Daily VOC Impact scores (indicating greater impact) than patients with lower symptom severity, as defined by the PGI-S (p<0.001; **Table 4**)
- Effect sizes used to interpret the magnitude of difference in the daily scores are considered large (≥0.80)

Responsiveness

Correlation analyses

- Change in SCPD-S Daily VOC Impact scores for Scale 1 were correlated with change in symptom severity (r=0.41); the strength of these relationships exceeded the threshold considered indicative of adequate responsiveness
- Change in Scale 2 scores were not as strongly correlated with change in symptom severity (r=0.27)

Mean Change Analyses (**Table 5**)

- For both scales, significant differences in mean SCPD-S Daily VOC Impact change scores were observed across groups of patients defined by change in symptom severity (p<0.001). The greatest amount of improvement in SCPD-S scores was observed for patients whose change in PGI-S indicated improvement

Table 3. Convergent Validity of SCPD-S Daily VOC Impact Score

Criterion measure	Scale 1 Coefficient	Scale 2 Coefficient
VOC pain at its worst	0.49	0.44
VOC paint at its least	0.44	0.36

Scale 1 N = 299; Scale 2 N = 296.

Table 4. Known-Groups Validity of the SCPD-S Daily VOC Impact Score

	Scale 1		Scale 2	
	N	Mean (SD)	N	Mean (SD)
PGI-S Group[1]				
Higher symptom severity	90	74.2 (18.94)	90	63.1 (25.85)
Lower symptom severity	209	48.4 (23.98)	206	36.4 (28.55)
ES		1.15		0.97
F (P-value)		82.01 (P<.001)		58.16 (P<.001)

[1] Higher symptom severity: PGI-S = Extremely, very, or markedly severe; Lower symptom severity: PGI-S = Not at all, minimally, mildly, or moderately severe.

Table 5. Responsiveness of the SCPD-S Daily VOC Impact Score, Mean Change

	Scale 1			Scale 2		
	N	Mean Change (SD)	ES	N	Mean Change (SD)	ES
Change in PGI-S						
Improved	58	-16.5 (21.04)	-0.75	58	-14.2 (23.25)	-0.46
No Change	59	-9.4 (15.83)	-0.42	59	-7.1 (25.17)	-0.25
Worsened	46	9.2 (19.62)	0.40	44	14.2 (29.46)	0.50
F (P-value)		24.7 (P<0.001)			15.9 (P<0.001)	

Patients were grouped according to change in between the first day and the middle day of the first VOC. Since higher SCPD-S scores indicate greater impact, a negative change score indicates improvement (i.e., reduced impact), while a positive change score indicates worsening (i.e., increased impact).

Psychometric Properties of the SCPD-S 7-Day VOC Impact and VOC Experience Impact Aggregate Scores

- Results of psychometric analyses of the SCPD-S 7 Day VOC Impact Aggregate and SCPD-S VOC Experience Impact Aggregate scores are summarized in **Table 6**
  - Scale 1, but not Scale 2, of the VOC Experience Impact Aggregate score showed adequate psychometric properties
  - Psychometric properties for both scales of the 7-Day VOC Impact Aggregate were not satisfactory

Table 6. Summary of Psychometric Analyses of the SCPD-S VOC Impact Aggregate Scores

	SCPD-S 7 Day VOC Impact Aggregate		SCPD-S VOC Experience Impact Aggregate	
	Scale 1	Scale 2	Scale 1	Scale 2
Test-retest reliability	Unsatisfactory	Unsatisfactory	Satisfactory	Satisfactory
Convergent validity	Satisfactory	Satisfactory	Satisfactory	Satisfactory; notably weaker than Scale 1
Known-groups validity	Borderline	Borderline	Satisfactory	Borderline; notably weaker than Scale 1
Responsiveness	Borderline	Unsatisfactory	Borderline	Borderline

Acknowledgements

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Disclosures

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