Factors Associated with Longitudinal Trajectories of Hydroxyurea Adherence among Individuals with Sickle Cell Disease: A Group-Based Trajectory Modeling Study

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INTRODUCTION

- Sickle cell disease (SCD) is a rare disorder caused by a mutation in the beta hemoglobin, which results in sickled red blood cells.
- While overall hydroxyurea adherence is low (10%-38%), examining longitudinal real-world trajectory adherence patterns may help identify intervention timepoints and targeted patient characteristics.
- The objective of this study was to identify distinct longitudinal hydroxyurea adherence trajectories among individuals with SCD enrolled in Texas Medicaid and to examine sociodemographic and clinical factors associated with trajectory group membership.

METHODS

Data source/ study design	• Retrospective analysis of Texas Medicaid data (01/2016-08/2023)
Inclusion/exclusion criteria	Inclusion criteria: • Individuals with ≥3 inpatient or outpatient claims for SCD on separate days during the study period. • ≥1 hydroxyurea claim without a claim in the 6 months pre-index period. • Aged 2-63 on index date (first claim for hydroxyurea) • Continuously enrolled for at least 6 months pre- and 12 months post- index in Texas Medicaid. Exclusion criteria: • Individuals with a diagnosis associated with a non-SCD indication during the pre-index period. • Individuals who had received hematopoietic stem cell transplantation during the pre-index period.
Adherence measure	• Adherence was measured as monthly proportion of days covered (PDC) over the 12-month post-index period.

Group-based trajectory modeling (GBTM)	• GBTM was used to identify trajectories of hydroxyurea adherence and estimate the proportion of individuals in each trajectory group.
	• Continuous PDC for each 30-day period over the 12 months was the model input.
	• Models with 2-6 trajectories were estimated and the best model fit was determined based on:
	  • Minimum predicted group proportion (>10%).
	  • Bayesian information criteria (lowest = better fit).
	  • Bayes factor with >10 indicating strong improvement over the previous model.
	  • Clinical interpretability.

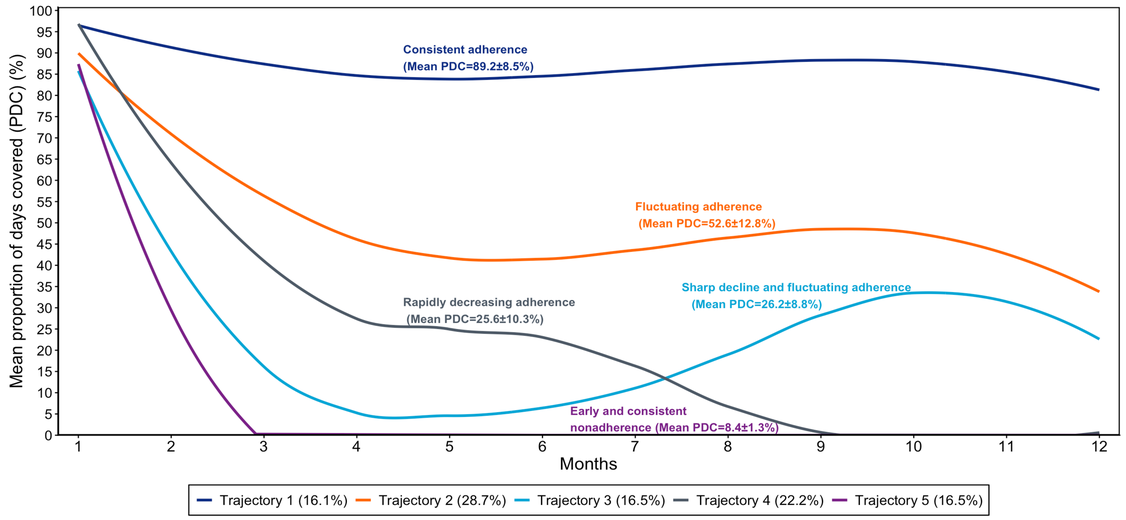
Outcome	• Hydroxyurea adherence trajectory group membership.
Independent variables	• Sociodemographic and clinical characteristics assessed during the pre-index period.
Statistical analysis	• Multinomial logistic regression was used to evaluate the association between sociodemographic and clinical characteristics and hydroxyurea adherence group membership. • P<0.05 was considered statistically significant.

RESULTS

- We included 1,246 individuals with SCD (mean age: 18.1±12.7), of which 50.8% were females.
- Monthly PDC declined from 98.6±8.7% in month 1, to 43.5±44.3% in month 2, and 30.5±40.9% in month 12 (Table 1).
- Five unique hydroxyurea adherence trajectories were identified: Consistent adherence (16.1%), Fluctuating adherence (28.7%), Sharp decline and fluctuating adherence (16.5%), Rapidly decreasing adherence (22.2%), and Early and consistent nonadherence (16.5%) (Figure 1).
- Early trough adherence timepoints occurred at months 2, 3, and 5 (Figure 1).
- Compared to children aged 2-15 years, those in other age groups (16-21, 22-34, and ≥35 years had significantly higher odds of membership (adjusted odds ratio (aOR) range: 2.25-8.72, p<0.02) in the lower adherence trajectories (Figure 2).
- Additionally, an increasing number of VOC events in the pre-index period was significantly associated with higher odds of membership (aOR range: 1.24-1.41, p<0.03) in the lower adherence trajectories compared to the consistent adherence trajectory (Figure 2).

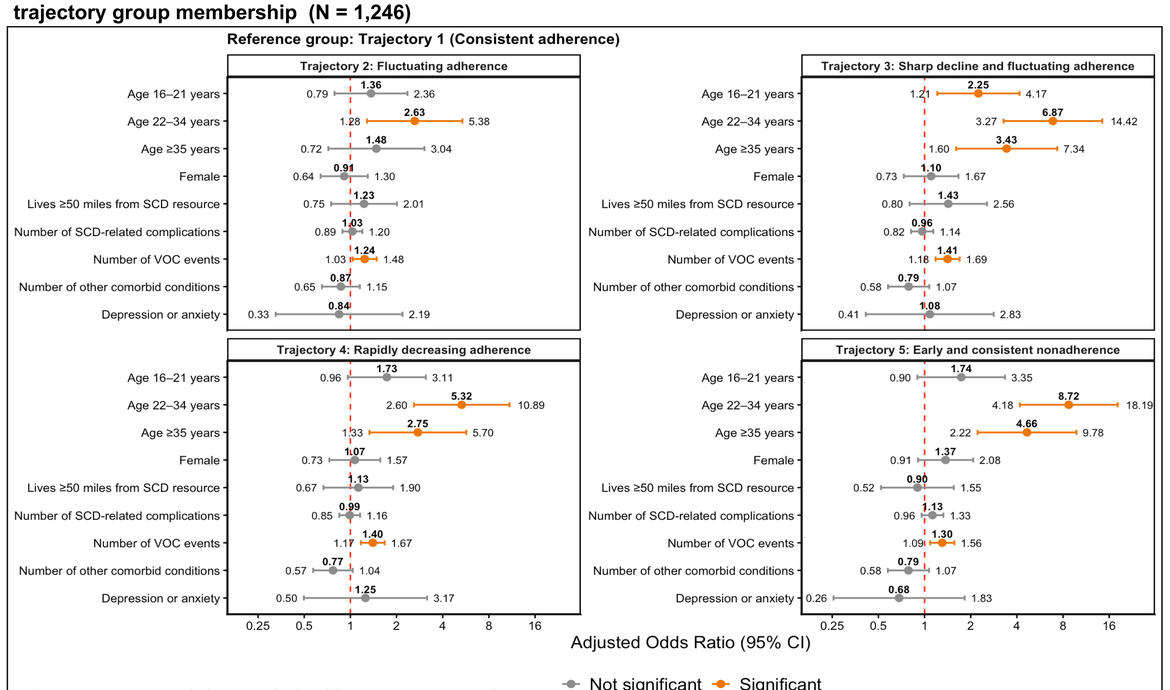
RESULTS

Figure 1: Longitudinal hydroxyurea adherence trajectories among individuals with SCD (N = 1,246)



Individualized and timely interventions should be tailored to young adults and adults, especially those who are transitioning to adult care, and those experiencing frequent VOC.

Figure 2: Multinomial logistic regression analysis of factors associated with longitudinal hydroxyurea adherence trajectory group membership (N = 1,246)



Reference: Age 2-15 years; male; lives <50 miles from SCD resource; no depression/anxiety

Odds ratio <1 indicates *lower odds* of membership in the comparison trajectory than in the reference trajectory (i.e., consistent adherence); better adherence.
Odds ratio >1 indicates *higher odds* of membership in the comparison trajectory than in the reference trajectory (i.e., consistent adherence); lower adherence.

Table 1. Monthly and overall adherence to hydroxyurea (N = 1,246)

Measure	Mean PDC	PDC≥80%
	Mean±SD	n (%)
Month		
1	98.6±8.7	1,215 (97.5)
2	43.5±44.3	459 (36.8)
3	41.3±43.0	399 (32.0)
4	38.3±41.9	356 (28.6)
5	35.3±41.6	329 (26.4)
6	36.7±41.8	338 (27.1)
7	34.9±41.6	328 (26.3)
8	33.4±41.5	320 (25.7)
9	32.8±41.2	312 (25.0)
10	32.6±41.2	312 (25.0)
11	31.3±41.1	300 (24.1)
12	30.5±40.9	292 (23.4)
Overall adherence		
Overall	40±27.8	167 (13.4)

LIMITATIONS AND STRENGTHS

Limitations

- GBTM assumes homogeneity within trajectory groups, which may oversimplify adherence patterns and lead to some misclassification.
- Prescription claims was used in estimating adherence, which does not translate to actual usage

Strengths

- Real world study using more recent data with up to 1,246 individuals with SCD.
- Distinct hydroxyurea adherence trajectories and timepoints for interventions were identified.

CONCLUSION

- Unique adherence trajectory patterns with critical time points for intervention were observed.
- Our findings highlight the need for individualized and timely interventions to address barriers to hydroxyurea adherence, especially among individuals transitioning to adult care and those experiencing frequent VOC.

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