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Transition to Adult Care in Sickle Cell Disease: A longitudinal Study of Clinical Characteristics and Disease Severity

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Abstract

Background.—Sickle cell disease (SCD) is a chronic blood disorder in which mortality has increased for adolescents and young adults (AYA).

Procedure.—A longitudinal analysis of medical records was conducted to describe the clinical course among AYAs (ages 12–27 years) during transition to adult care. Measures included sociodemographic, complications, SCD severity (modified pediatric SCD severity index), comorbidities, and transfer. Group-based trajectory modeling (GBTM) to identify subgroups with distinct severity trajectories and chi-square and unpaired student t-test to explore subgroup differences were used.

Results.—Overall, 339 AYAs (97% black, 56% male, 69% hemoglobin SS) had 10848 clinic, 3840 hospital, and 3152 emergency department visits. Complications included vaso-occlusive crises (80%) and acute chest syndrome (41%). Comorbidities included depression (19%) and anxiety (14%). Most AYAs transferred to adult care (n=220) at 19 years. Fourteen AYAs died, 10

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Conflict of Interest

within seven years from transfer. GBTM identified both stable and increasing severity trajectory groups: stable-low (n=31, 23%), stable-medium (n= 61, 46%), stable-high (n=6, 5%), low-increasing (n=13,10%), and medium-increasing (n= 22,17%). AYAs with increasing severity (25%) were older, lived closer to the clinic, and had higher risk for SCD complications and comorbidities. They had less pediatric clinic visits, however, they were more likely to transfer and remain longer in adult SCD care.

Conclusions: Whereas most AYAs had stable severity, nearly a quarter had increasing severity, over time. AYAs with increasing severity had more complications, were more likely to transfer to adult care, and demonstrated higher and longer adult SCD care utilization compared to AYAs with stable severity.

Keywords

Sickle cell disease; adolescent; young adult; transition to adult care; severity; complications

Introduction

Landmark advances in pediatric sickle cell care have resulted in most children with sickle cell disease (SCD) surviving into adulthood.^{1,2} However, improvements in child health outcomes have not yet been experienced by adults. For example, mortality rates among children with SCD have significantly declined over the past four decades, whereas mortality rates among individuals with SCD over 19 years of age continue to rise.^{1,3} Of concern is the substantive increase in mortality during the adolescent and young adult years, coinciding with the time of transfer from pediatric to adult care. A sharp increase in mortality rates from 0.6/100,000 between ages 15 and 19 years to 1.4/100,000 between ages 20 to 24 years has been demonstrated.³ Similarly, a follow up on the Dallas Newborn Cohort (n=940) found that all new seven deaths since 2001 occurred among those who were older than 18 years and that six of these seven deaths occurred at a mean of 1.8 years after transfer to adult care.²

Little is known about aspects of the disease course that might be contributing to the increase in mortality during the transition period for adolescents and young adults (AYA) with SCD. The leading cause of death among the Dallas Newborn Cohort included acute chest syndrome and multi-organ failure syndrome.² Darbari and colleagues found that the frequency of vaso-occlusive crises increased with age among adolescents with SCD.⁴ Adolescents and young adults with SCD were also found to be at risk for high rates of depression and anxiety,^{5,6} with reported depression rates as high as 45% in adolescents⁶ and 27.6% in adults.⁷ The purpose of this study was to provide a longitudinal description of the clinical characteristics and disease severity among AYAs with SCD during transition from pediatric to adult care.

Methods

Design and Setting

A longitudinal retrospective analysis of electronic health records of AYAs who received care at a comprehensive sickle cell program in the Southeast U.S. between January 1, 1989 and

July 30, 2015 was conducted. The sickle cell program provides care to over 900 individuals with SCD. A transition program was formally established in 2012 where a multidisciplinary team provides education on SCD management and health care navigation skills to AYAs and their caregivers to facilitate their transition to adult care. The goal is to transfer patients when they are at least 18 years old and have graduated high school. Transfer might be delayed up to age 20 years if patients have not graduated high school or are in their first year at college.

Study Population and Database

The institutional review board approved the study and waived participant's consent and HIPPA authorization. Inclusion criteria for AYAs (12–27 years) were: (1) had SCD (hemoglobin SS (SS); sickle hemoglobin C (SC); sickle/beta plus thalassemia (Sβ+); or sickle/beta zero thalassemia (Sβ°) genotype) and (2) had a minimum of two pediatric SCD clinic visits during adolescence (12–18 years), including at least one visit after age 15 years to ensure initial integration in pediatric SCD care. Age 12 to 27 years was selected to ensure that transition to adult care was captured.

Patients meeting the inclusion criteria were identified through the Duke Enterprise Data Unified Content Explorer (DEDUCE) research portal- a data extraction system that identifies patient cohorts and provides access to clinical data stored in the organizational data warehouse.⁸ Data across the health system's three hospitals and 29 outpatient clinics are available to institution-affiliated researchers.

Measures

Sociodemographic characteristics.—Sociodemographic characteristics, including residence location, were extracted. Distance in miles between the residence and the SCD clinic was calculated based on the United States postal service (USPS) 5-digit zip code.

SCD specific measures.—SCD specific measures included genotype, SCD complications, disease severity, and prescribed treatments. Data were extracted from data files associated with clinic visits, emergency department (ED) visits, and hospitalizations. Genotype was extracted from physician notes.

SCD complications included vaso-occlusive crises (VOC), acute chest syndrome (ACS), stroke or cerebral infarct, among others. Complications were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)⁹ codes supplemented by diagnoses names from problem and diagnoses lists associated with clinic, ED, and hospital visits for a more comprehensive capture of diagnoses. Complications were binary coded as present (if they occurred at any visit) or absent (if they never occurred at any visit).

Age-related mean severity scores were calculated using a modification of a pediatric severity index previously used to differentiate between mild, moderate, and severe disease.¹⁰ In its original form, the severity index consists of 12 weighted items with a total score of 285 based on the lifetime cumulative incidence of SCD complications, such as avascular bone necrosis (AVN), cerebral infarcts or vasculopathy, and acute hepatic sequestration; the

cumulative incidence of ACS and VOC episodes over two years; and laboratory values.¹⁰ The scale was modified for this study to exclude laboratory values because of missing data. The authors considered this to be acceptable because in the original validation study, only seven (8%) participants had scores for laboratory values.¹⁰ The lifetime cumulative incidence of acute hepatic sequestration was also eliminated because there is no ICD-9-CM code for acute hepatic sequestration. The modified version of the scale had a score range of 0–200 (Supplementary Table S1). Because two years of data on VOC and ACS episodes were needed, age-related mean severity scores were calculated between ages 14 and 27 years (14 data points).

Self-reported prescribed medications were extracted from the outpatient medications reconciliation record at the last outpatient visit. Medications were classified into: non-narcotic pain management (analgesics/ analgesic combinations/ non-steroidal anti-inflammatory), extended release narcotics, short acting narcotics, and hydroxyurea. Blood transfusions were identified from diagnoses lists using ICD-9-CM codes, procedure lists using CPT codes, and physician orders to capture all possible blood transfusions.

Comorbidities.—Selected comorbidities included asthma; mental health conditions such as anxiety and depression; and disabilities. Comorbidities were identified using ICD-9-CM codes supplemented by diagnoses names from problem and diagnoses lists associated with the visit for a more comprehensive capture of diagnoses.

Transfer related measures.—Transfer from pediatric to adult care was defined as the age at which the AYAs had their first adult sickle cell clinic appointment. Mean time in years was calculated from the last pediatric to the first adult sickle cell clinic visit. Continuity of care was examined as the frequency of clinic appointments and mean duration in care in years.

Procedures

Using the DEDUCE portal, filters with the inclusion criteria were sequentially applied to identify the sample and extract data on study measures. Electronic health records were reviewed to extract the SCD genotype. SAS statistical software (version 9.4, SAS Institute, Inc., Cary, NC) was used for data management and analyses.

Data Analyses

To describe disease severity over time, group-based trajectory modeling with Proc Traj¹¹ was used. This approach allows for (1) the identification of latent but distinctive groups of individuals within a heterogeneous population who follow a similar pattern on an outcome (disease severity) over time or age and (2) the determination of the shape of the trajectory for each of these groups.^{12–14} Because the data were positively skewed following a Poisson distribution, the zero-inflated Poisson (ZIP) model was used^{15,16} to analyze the conditional distribution of the severity scale data over ages 14 to 27 years. An extension of the group-based trajectory modeling using 95% confidence intervals (95%CI) on trajectories was used.¹²

Model selection occurred over two stages. In stage one, the number of trajectory groups that best describe the data was determined by fitting models with predetermined number of groups (two to six) using the quadratic order of the polynomial and comparing the fit indices of the Bayesian information criteria (BIC).¹⁷ The model with the maximum BIC score (BICs were all negative) was selected. In stage two, the preferred order of the polynomial specifying the shape of each trajectory was determined based on different iterations and the model with the maximum BIC score was selected.¹⁷ Whenever two models had close BIC scores, Jeffreys's scale of evidence for Bayes factors (approximated by calculating the exponential of the difference between the two BICs) was used to determine which model was better supported.¹⁷ The adequacy of the final selected model was tested by examining the posterior probabilities of group membership and setting the limit to at least 0.7 for all groups.¹⁷

Chi-square and unpaired student t-test were used to describe subgroup differences among (1) Patients with different severity trajectory groups (2) Patients who were eligible to transfer based on their age (≥ 19 years old) and transferred compared to patients who were eligible to transfer but did not transfer; and (3) Patients who died compared to patients who were still alive during the study. Statistical significance was set at $p \leq 0.05$ and 95% CI.

Results

Sociodemographic Characteristics

The sample consisted of 339 AYAs with 10848 pediatric and adult SCD clinic visits, 3840 hospitalizations, and 3152 ED visits. Patients were born between 1977 and 1999 and had data over a mean duration of 11.4 years (95%CI 10.9–11.9). At the last data point, 325 (96%) patients were alive (mean age= 24.5 years; 95%CI 23.9–25.0), whereas 14 (4.1%) had died (mean age= 24.6 years; 95%CI 22.2–26.9). Most patients were black (n=328, 96.8%), male (n=188, 55.5%), and single (n=292, 86.1%). Patients lived at a mean of 48.7 miles (95%CI 45.3–52.1) from the clinic (Table 1).

SCD-Specific Measures

Most patients had SS genotype (68.7%). Vaso-occlusive crises and ACS episodes were the most common complications, with 80% and 40.7% respectively. Approximately 34% of patients had a diagnosis of chronic pain, 22% had a diagnosis of avascular necrosis, and 22% had a diagnosis of cerebral infarcts/ vasculopathy (Table 1).

Age-related mean modified SCD severity scores were calculated between ages 14 and 27 years (n=339). Overall, patients had stable severity between ages 14 and 17, gradually increasing severity with age between ages 18 and 25 years, and stable severity between ages 25 and 27 years (Fig. 1A).

To identify the subgroups of patients with different severity trajectories, group-based trajectory modeling was used. To ensure model stability, patients who had severity scores for at least 10 years between ages 14 and 27 years (n=133, 39%) were included in this analysis. The group-based trajectory modeling indicated that a five-group model best fit the data (Supplementary Table S2) with three stable and two increasing severity trajectory groups

(Fig. 1B): Group 1 (n=31, 23.3%), Group 3 (n= 61, 45.9%), and Group 5 (n=6, 4.5%) had a stable-low, stable-medium, and stable-high severity trajectory, respectively; whereas Group 2 (n=13, 9.7%) and Group 4 (n= 22, 16.5%) had low-increasing and medium-increasing severity trajectories, respectively.

Prescribed Treatments.—Overall, 261 (77%) patients self-reported taking non-narcotic medications, whereas 196 (58%) and 38 (11%) reported taking narcotics and extended-release narcotics, respectively. Approximately 63% (n=212) self-reported taking hydroxyurea (173 had SS, 28 had SC, 4 had Sβ+, and 7 had Sβ° genotypes). A quarter of patients (n=86) received blood transfusions.

Comorbidities.—Asthma occurred among 26% of patients. A variety of mental health conditions were prevalent, with depression (18.6%) and anxiety (14.2%) as the most common (Table 1). Seven (2%) patients were diagnosed with suicidal ideation, four of whom attempted suicide. All four patients were black; had SS genotype; and were diagnosed with cerebral infarcts or vasculopathy, chronic pain, major depression, and anxiety. Only one patient was diagnosed with suicidal ideation prior to suicide attempt.

Transfer to Adult Care

Of the 339 patients, 293 (86%) were eligible to transfer based on age (i.e. 19 years old), whereas 46 (14%) were 18 years or younger making them ineligible for transfer to adult care. Of the 293 patients who were eligible to transfer, 220 (75%) transferred at a mean age of 18.9 years (95%CI 18.7–19.1). The mean time from the last pediatric to the first adult SCD clinic visit was 0.78 years (95%CI 0.5–1.1). Patients who transferred remained in adult SCD clinic care for a mean of 5.2 years (95%CI 4.8–5.6) with a mean of 5.3 clinic visits per year (95%CI 4.5–5.6).

Of the 339 patients, 116 (34.2%) did not transfer to adult care within the health system. Their mean age was 17.3 years (95%CI 17.1–17.6). They were in pediatric SCD clinic care for a mean of 5.3 years (95%CI 4.9–5.6) with a mean of 4.3 visits per year (95%CI 3.3–5.4).

Mortality.—Fourteen patients (4.1%) died during the study, most were male (n=8) and had SS genotype (n=11). Six patients had data on severity with a median severity score of 50 (95%CI 16.1–61.4). Four patients died between the ages 18 and 21 years while in pediatric care. Ten patients died after transfer to adult care. Their median age at transfer was 19 years (95%CI 18.4–20.2). They had a median of seven years (95%CI 5.1–9.5) between transfer and death and a median of 5 visits per year (mean=5.4, 95%CI 3.4–7.4) in adult care.

Subgroup Differences in Severity.—Compared to patients with stable severity trajectories (Fig. 1B; Groups 1, 3, and 5), patients with increasing severity trajectories (Fig. 1B; Groups 2 and 4) were more likely to be married, older, and lived closer to the clinic. They were at higher risk for SCD complications, specifically acute kidney disease (RR=6; 95%CI 2.8–12.6), jaundice (RR=4.2; 95%CI 2.1–8.5), pulmonary hypertension (RR=3.6; 95%CI 1.8–9.1); AVN (RR=3.2; 95%CI 2.1–4.9), and chronic pain (RR=2.3; 95%CI 1.7–3); receiving extended release narcotics (RR=5; 95%CI 2.6–9.9); and depression (RR=2.5; 95%CI 1.6–3.8) and anxiety (RR=2.4; 95%CI 1.4–4.1). They had less pediatric SCD clinic

visits at age 18 years, however, they were more likely to transfer to adult care, had more adult SCD visits overall, and remained longer in adult SCD care after transfer (Tables 2 and 3). There were no significant differences between patients with increasing severity trajectories compared to patients with stable severity trajectories on SCD genotype; other SCD complications including VOCs; receiving hydroxyurea; pediatric clinic visits before age 18 years; and duration in pediatric care.

Subgroup Differences in Transfer to Adult Care.—Compared to patients who did not transfer, patients who transferred were older and lived closer to the SCD clinic. They were at higher risk for SCD complications, specifically jaundice (RR=5.6; 95%CI 1.4–22.9), chronic pain (RR=5.4; 95%CI 2.5–11.8), pulmonary hypertension (RR=5.3; 95%CI 1.3–21.6), AVN (RR=3.5; 95%CI 1.6–7.8); ACS (RR=3.4; 95%CI 1.9–6.2), and VOC (RR 1.5; 95%CI 1.2–1.8); receiving extended release narcotics (RR=3.9; 95%CI 1.2–12.2), narcotics (RR=2.6; 95%CI 1.7–3.8), blood transfusions (RR=2.2; 95%CI 1.2–4), and hydroxyurea (RR=1.5; 95%CI 1.1–1.9); and depression (RR=9.1; 95%CI 2.3–36.5) and anxiety (RR=4.7; 95%CI 1.5–14.5). They had higher mean annual pediatric SCD clinic visits, especially during older adolescence, and were in pediatric care for a longer duration (Tables 4 and 5). There were no significant differences between patients who transferred and patients who did not transfer on SCD genotype, other complications, other comorbidities, and pediatric clinic visits in early adolescence.

Subgroup Differences in Mortality: Patients who died (n=14) spent less time in pediatric clinic care (mean=4.6 years, 95%CI 3.7–5.6), however, they had a higher mean number of annual pediatric clinic visits (mean=9.3 visits; 95%CI 6.3–12.3) compared to those who were alive (n=324, mean=6 years in pediatric clinic care, 95%CI 5.7–6.1; mean annual pediatric clinic visits =5.4, 95%CI 4.8–6.1). There were no differences in sociodemographic characteristics, genotype, complications, severity group, or morbidity between patients who died and patients who were still alive.

Discussion

This study described the clinical characteristics and disease severity during transition to adult care among a large sample of AYAs with SCD. Whereas most patients had a relatively stable disease severity trajectory into young adulthood, for a quarter of patients, disease severity increased with age. Taking into consideration the limited availability of validated SCD severity measures and the potential limitation of using a modified version of a severity index to measure severity, these findings still have preliminary implications for identifying patients who might be at risk for worsening disease course with increasing age. AYAs with increasing severity lived closer to the SCD clinic, were more likely to transfer to adult care, and demonstrated higher and longer use of adult SCD care compared to AYAs with stable severity. Importantly, SCD genotype was not associated with increasing severity, however, certain complications including acute kidney disease, jaundice, and pulmonary hypertension were more likely in patients with increasing severity trajectories, emphasizing the variability in the phenotypic presentation of SCD and the need to frequently evaluate the clinical course of patients to identify and intervene for patients at risk for increased disease severity with increasing age.

Mental health conditions, including depression and anxiety, were common in this sample and four patients attempted suicide. Although there were no age-related patterns; SS genotype; high disease severity; and diagnoses of depression, chronic pain, and cerebral infarct were shared characteristics among these patients. Because the rate of depression and suicidal ideation were determined retrospectively using ICD-9-CM codes, it is possible that other patients had undiagnosed depression and suicidal ideation. The implications from these findings are significant given the rate of depression and the association of depression with increasing severity in this sample and the documented high rate of depression in SCD in general.^{6,7} Health care professionals need to frequently screen AYAs with SCD; particularly AYAs with high disease severity, chronic pain, and cerebral infarct; for mental health conditions including depression, anxiety, and suicidal ideation. In a busy clinic with a complex, chronically-ill patient pool, identifying patients with mental health conditions might be challenging and will require systematic interventions for screening and referral to mental health services. In this high-risk patient population, however, appropriately addressing mental health conditions might decrease disease burden and improve health outcomes.

Most patients who were eligible for transfer based on age, transferred to adult care within one year from their last pediatric clinic visit. The time between the first adult clinic visit and the last pediatric clinic visit was slightly more than the 3–6 months consensus period for successful transition,¹⁸ indicating the need for quality improvement initiatives at our center to improve the lag time between pediatric and adult care. Patients who transferred were more likely to have a complicated disease course and to be engaged in pediatric care, particularly during late adolescence. These findings might indicate that early engagement of patients in care, particularly during late adolescence and before transfer to adult care might be as an important factor for transitioning and engaging patients in adult care. Although it might reflect provider vigilance with patients with complicated disease course, it is encouraging that patients who demonstrated a complicated disease course were more likely to transfer and engage in adult care.

Importantly, 14 AYAs died during the study, which is similar to previous data that showed a risk of death beginning in the early twenties.^{2,3} Deaths occurred among patients who had transferred to adult care with a median of seven years between transfer and death. This is longer than was reported in the Dallas Newborn Cohort study (1.8 years)² and might be due to regional variations in care. These patients demonstrated less duration but more pediatric clinic visits compared to those who lived. No other differences were found. These findings need to be interpreted with caution given the small number of patients in this group.

Limitations

The study had limitations. First, data were limited to one health care system and did not include any potential visits at other institutions. In addition, disease burden might be under-represented in this sample when compared to individuals not affiliated with a comprehensive SCD center. Future research should utilize more comprehensive datasets, including state and national level data that might provide a more comprehensive picture of disease burden among AYAs with SCD. Second, this study relied on retrospective ICD-9-CM codes to

determine disease complications and comorbidities. However, we supplemented ICD-9-CM codes associated with each visit with diagnoses names from problem and diagnoses lists associated with that visit to ensure a more comprehensive capture of diagnoses. Third, undiagnosed mental health conditions in this population are likely and relying on retrospective diagnoses might have underestimated the actual rate of mental health conditions in this sample. Fourth, due to missing data on laboratory values, a modification of the severity index was necessary to calculate severity scores for this sample. A larger sample would be required to validate the modified version of the severity index. Fifth, disease severity was examined among 39% of the sample, which might further limit the generalizability of the findings. Despite these limitations, this study addresses a critical gap in knowledge by describing the clinical course and the trajectories of disease severity among a sample of AYAs with SCD during their transition to adult care.

Conclusions

Although most patients had a stable disease severity trajectory, a quarter had increasing severity with age. Health care professionals need to closely monitor for the occurrence of disease complications particularly during the transition period, and educate patients on prevention, appropriate self-management, and when to seek medical care. For AYAs with SCD, their disease course was further complicated with high rates of mental health conditions, including depression and anxiety. Therefore, routinely screening AYAs for these conditions should be considered. Ongoing efforts are needed to develop interventions that might benefit AYAs with a complicated disease course to improve their health outcomes and their transition to adult care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations table

SCD	Sickle cell disease
AYA	Adolescent and young adult

SS	Hemoglobin SS genotype
SC	Sickle hemoglobin C genotype
Sβ+	Sickle/beta plus thalassemia genotype
Sβ°	Sickle/beta zero thalassemia genotype
ED	Emergency department
VOC	Vaso-occlusive crisis
ACS	Acute chest syndrome
AVN	Avascular bone necrosis
95%CI	95% confidence interval
BIC	Bayesian information criteria

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FIGURE 1.
A. Age-related mean modified severity score (ages 14–27 years; n=339)
B. Age-related Disease Severity Trajectories (ages 14–27, n=133)
Group 1 (n= 31, 23.3%): stable-low severity trajectory group
Group 2 (n=13, 9.7%): increasing-low severity trajectory group
Group 3 (n= 61, 45.9%): stable-medium severity trajectory group
Group 4 (n=22, 16.5%): increasing-medium severity trajectory group

Group 5 (n=6, 4.5%): stable-high severity trajectory group

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TABLE 1
Sample characteristics

N=339	n	(%)	Mean (95%CI)
Sociodemographic			
Years in dataset	339	(100)	11.4 (10.9–11.9)
Age Alive, years	325	(95.9)	24.5 (23.9–25.0)
Age at death, years	14	(4.1)	24.6 (22.2–26.9)
Sex, Male	188	(55.5)	
Race, Black	328	(96.8)	
Marital status, Single	292	(86.1)	
Distance from clinic, miles	312	(92)	48.7 (45.3–52.1)
Genotype			
Hemoglobin SS	233	(68.7)	
Sickle hemoglobin C	82	(24.2)	
Sickle/Beta plus thalassemia	13	(3.8)	
Sickle/Beta zero thalassemia	11	(3.2)	
Sickle cell complications			
Vaso-occlusive crisis	271	(80.0)	
Acute chest syndrome	138	(40.7)	
Pain, chronic	117	(34.5)	
Avascular necrosis	75	(22.1)	
Cerebral infarcts/ vasculopathy	76	(22.4)	
Kidney disease, acute	40	(11.8)	
Kidney disease, chronic	26	(7.7)	
Jaundice	38	(11.2)	
Priapism	37	(10.9)	
Pulmonary hypertension	34	(10.0)	
Iron-overload, transfusion related	28	(8.3)	
Splenic sequestration	15	(4.4)	
Ulcer, lower extremity	7	(2.1)	
Pneumococcal meningitis/ septicemia	2	(0.6)	
Comorbidities			
Asthma	88	(26.0)	
Depression	63	(18.6)	
Anxiety	48	(14.2)	
Depression with anxiety	17	(5.0)	
Adjustment disorder with depression	17	(5.0)	
Attention deficit/ Attention deficit hyperactivity disorder	12	(3.6)	
Intellectual disabilities	7	(2.1)	
Suicidal ideation	7	(2.0)	
Suicide attempt	4	(1.2)	

TABLE 2

Difference in sociodemographic characteristics and clinic utilization between increasing severity trajectory groups and stable severity trajectory groups^a

	Mean (95%CI)	
	Increasing severity trajectory groups (n=35)	Stable severity trajectory groups (n=98)
Sociodemographic		
Age, years	28.8 (27.4–30.2)	25.0 (23.9–26.1)
Distance, miles	31.8 (21.5–42.0)	46.2 (40.4–52.4)
Sickle cell clinic utilization		
Pediatric clinic, visits at age 18 years	3.2 (1.6–4.8)	5.9 (4.0–7.7)
Years in adult sickle cell care	7.8 (7.0–8.5)	5.9 (5.1–6.7)
Adult clinic, overall visits per year	10.2 (8.2–12.2)	6.5 (4.9–8.1)

^aBased on 133 patients with at least 10 years in the dataset and comparing patients with increasing severity trajectory groups (n=35; Fig.1B, Groups 2 and 4) and stable severity trajectory groups (n=98; Fig.1B, Groups 1,3, and 5). Only statistically significant (p < 0.05, 95%CI) variables are reported.

TABLE 3

Relative Risk for increasing severity trajectory group by sociodemographic characteristics, sickle cell complications, treatments, comorbidities, and transfer to adult care^a

	No. (%) of patients Increasing severity trajectory groups		Relative Risk (95%CI) Increasing severity trajectory groups
	Yes (n=35)	No (n=98)	
Sociodemographic			
Married	8 (22.9)	2 (2.0)	11.2 (2.5–50.3)
Sickle cell complications			
Kidney disease, acute	17 (48.6)	8 (8.2)	6.0 (2.8–12.6)
Jaundice	15 (42.9)	10 (10.2)	4.2 (2.1–8.5)
Pulmonary hypertension	14 (40.0)	11 (11.2)	3.6 (1.8–9.1)
Avascular necrosis	25 (71.4)	22 (22.5)	3.2 (2.1–4.9)
Pain, chronic	30 (85.7)	37 (37.8)	2.3 (1.7–3.0)
Acute Chest Syndrome	30 (85.7)	47 (48.0)	1.8 (1.4–2.3)
Treatments			
Non-narcotic pain management	35 (100)	72 (73.5)	1.4 (1.2–1.5)
Narcotics, extended release	18 (51.4)	10 (10.2)	5.0 (2.6–9.9)
Narcotics	33 (94.3)	65 (66.3)	1.4 (1.2–1.7)
Blood transfusion	22 (62.9)	36 (36.7)	1.7 (1.2–2.4)
Comorbidities			
Depression	22 (62.9)	25 (25.5)	2.5 (1.6–3.8)
Anxiety	16 (45.7)	19 (19.4)	2.4 (1.4–4.1)
Transferred to adult care	35 (100)	71 (72.5)	1.4 (1.3–1.6)

^aBased on 133 patients with at least 10 years in the dataset and comparing patients with increasing severity trajectory groups (n=35; Fig.1B, Groups 2 and 4) and patients with stable severity trajectory groups (n=98; Fig.1B, Groups 1,3, and 5). Only statistically significant (p < 0.05, 95%CI) variables are reported.

TABLE 4

Difference in sociodemographic characteristics and clinic utilization between patients who transferred and patients who did not transfer to adult care^a

	Mean (95%CI)	
	Transferred n=220	Not transferred n=73
Demographics		
Age, years	26.5 (25.9–27.1)	22.9 (21.9–24.0)
Distance, miles	46.4 (42.3–50.6)	57.3 (48.9–65.7)
Sickle Cell Clinic utilization		
Years in pediatric sickle cell care	6.1 (5.9–6.4)	5.4 (4.9–6.0)
Pediatric clinic, overall visits per year	6.3 (5.5–7.1)	4.3 (2.9–5.6)
Pediatric clinic, visits at 14 years	5.7 (4.6–6.8)	3.6 (2.0–5.1)
Pediatric clinic, visits at 16 years	6.0 (5.0–7.1)	3.6 (1.9–5.4)
Pediatric clinic, visits at 17 years	6.0 (5.0–6.9)	3.8 (2.1–5.4)
Pediatric clinic, visits at 18 years	4.1 (3.2–5.0)	1.7 (1.0–2.5)

^aBased on 293 patients who were eligible to transfer to adult care (i.e. were ≥ 19 years old). Of those, 220 (75%) transferred, whereas 73 (25%) did not transfer. Only statistically significant (p < 0.05, 95%CI) variables are reported.

TABLE 5

Relative Risk for transfer to adult care by sickle cell complications, treatments, and comorbidities^a

	No. (%) of patients Transferred		Relative Risk (95%CI) for transfer
	Yes (n=220)	No (n=73)	
Sickle cell complications			
Jaundice	34 (16)	2 (3)	5.6 (1.4–22.9)
Chronic pain	98 (45)	6 (8)	5.4 (2.5–11.8)
Pulmonary hypertension	32 (15)	2 (3)	5.3 (1.3–21.6)
Avascular Necrosis	64 (29)	6 (8)	3.5 (1.6–7.8)
Acute Chest Syndrome	103 (47)	10 (14)	3.4 (1.9–6.2)
Cerebral infarcts	64 (29)	8 (11)	2.7 (1.3–5.3)
Vaso-occlusive crisis	189 (86)	42 (56)	1.5 (1.2–1.8)
Treatments			
Narcotics, extended release	35 (16)	3 (4)	3.9 (1.2–12.2)
Narcotics	152 (70)	19 (27)	2.6 (1.7–3.8)
Hydroxyurea	148 (67)	33 (45)	1.5 (1.1–1.9)
Blood transfusion	66 (30)	10 (14)	2.2 (1.2–4.0)
Comorbidities			
Depression	55 (25)	2 (3)	9.1 (2.3–36.5)
Anxiety	42 (19)	3 (4)	4.7 (1.5–14.5)

^aBased on 293 patients who were eligible to transfer to adult care (i.e. were ≥ 19 years old). Of those, 220 (75%) transferred, whereas 73 (25%) did not transfer. Only statistically significant (p ≤ 0.05, 95%CI) variables are reported.