MILLIMAN RESEARCH REPORT

A claims-based analysis of sickle cell disease: Prevalence, disease complications, and costs

Considerations for commercial and managed Medicaid payers

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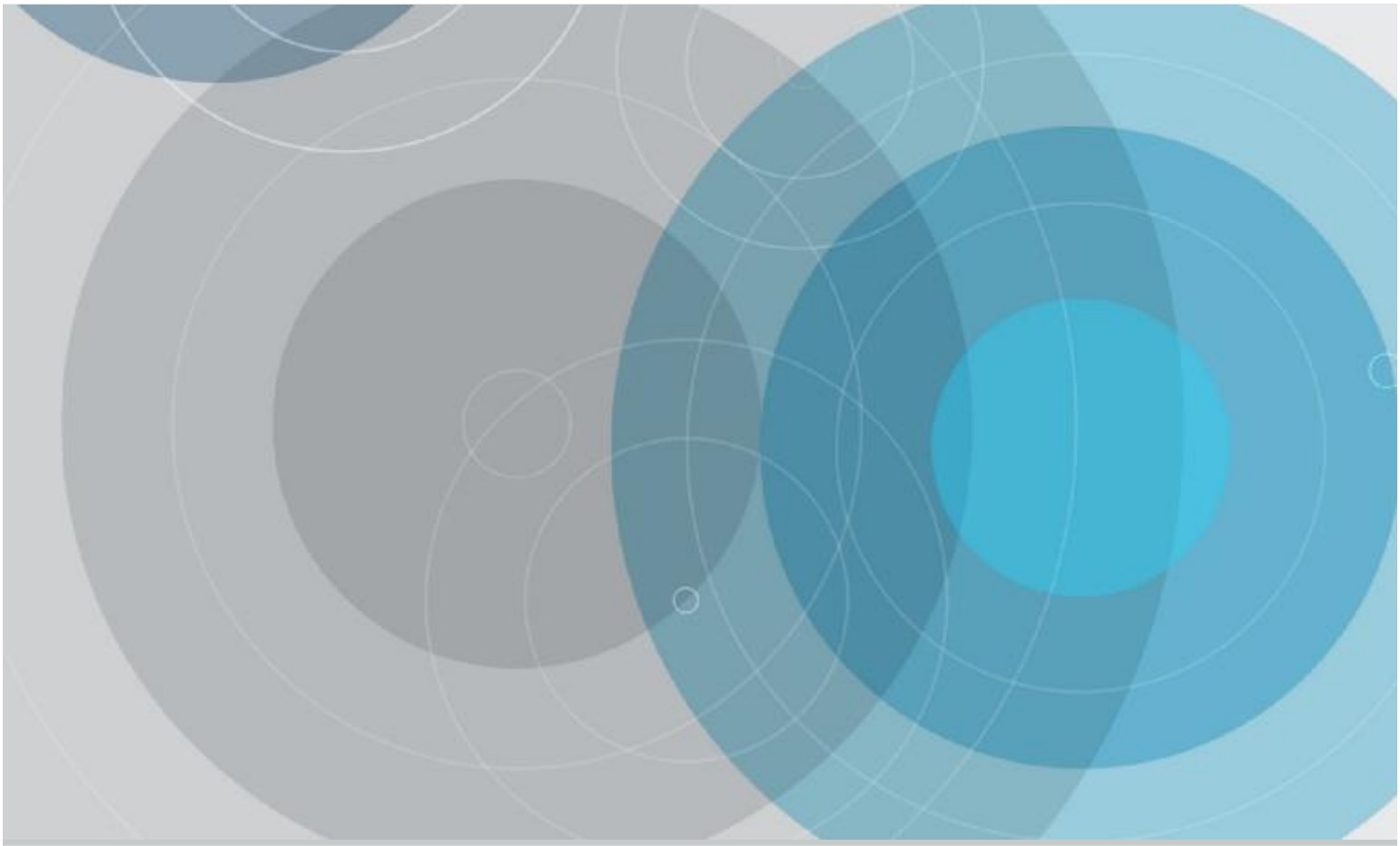

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Appendices A, B, and C can be found in supplemental materials and are available online.

EXECUTIVE SUMMARY

An estimated 100,000 people are living with sickle cell disease (SCD) in the United States as reported by the Centers for Disease Control and Prevention (CDC), based on research by Hassell published in 2010.[1] In recent decades survival into adulthood among individuals with SCD has been nearly universal in developed countries, due to diagnostic and prevention strategies such as newborn screening, penicillin prophylaxis, and pneumococcal vaccination.[2,3] However, increased survival among children with the disease has led to a significant clinical and economic burden in adults with SCD, as most of the morbidity and mortality caused by end-organ damage has shifted from childhood to adulthood.[4]

There has been little contemporaneous analysis of healthcare utilization and costs associated with SCD, and only limited information is available across payer types. In this analysis, we used real-world medical and pharmacy claims data for SCD patients covered either by commercial insurance or managed Medicaid to develop relevant diagnosis, utilization, and cost metrics by payer type. These included acute conditions requiring hospitalizations, chronic conditions, and treatments experienced by patients with SCD. We analyzed all-cause healthcare expenditures, as measured by the allowed amount reported on claims (amounts paid by both payer and patient combined), incurred over calendar year 2017, as well as utilization rates of healthcare encounters such as inpatient admissions and emergency department visits.

Using administrative claims data, we identified 3,014 commercial patients and 1,293 managed Medicaid patients with SCD in 2017. Our analysis stratified patients into three age groups (under 18, 18-34, and 35-64) to reflect the important changes in morbidity, healthcare utilization, and costs of SCD patients over time that are driven by the evolving clinical needs of SCD patients as they age. Among these patients, 34% of commercial and 41% of managed Medicaid SCD patients were children under age 18, and 37% of commercial and 25% of managed Medicaid SCD patients were adults ages 35 to 64.

Our review of these SCD patients' experience throughout 2017 found the following:

- **Chronic conditions for SCD patients accumulate with age.** Patients ages 35 and older reported the largest prevalence of one or more of the most common chronic conditions associated with SCD (67% of commercial and 84% of managed Medicaid). Furthermore, the number of comorbidities increased with age. The percentage of patients with three or more comorbidities doubled from ages 18-34 to ages 35-64, from 6% to 13% among commercial and 17% to 34% among managed Medicaid patients. By comparison, the percentage of SCD patients with acute conditions requiring hospitalization peaked in the 18-34 age group.
- **Many SCD patients are not under the care of hematologists.** Access to nonemergency outpatient care by hematologists, measured by outpatient evaluation and management visits billed by professionals with a provider specialty of hematology, was observed for less than half of SCD patients. Sixty-five percent of commercial and 59% of Medicaid SCD patients did not have a single outpatient hematologist visit during the year.
- **Utilization rates of existing treatments for SCD are low.** Two disease-modifying therapies that prevent and/or treat acute and chronic complications of SCD are hydroxyurea (HU) and chronic blood transfusions.[5,6]
    - HU, which raises hemoglobin F and hemoglobin levels and decreases the rate of vaso-occlusive crises (VOCs) by 50%, is the only drug that has been proven effective in reducing the frequency of pain episodes.[7] Moreover, long-term HU treatment also is associated with decreased mortality in symptomatic patients with SCD compared with patients receiving shorter-term HU or no HU. However, multiple studies have shown that HU treatment rates for patients with SCD are low and adherence is poor due to a number of patient, provider, and systems-level barriers in real-world clinical practice.[8] In our analysis, we found only 28% of commercial and 46% of managed Medicaid SCD patients filled at least one prescription for the drug in 2017. Furthermore, 40% of commercial and 43% of managed Medicaid HU users reported at least one 45-day or longer gap in treatment.
    - Chronic red blood cell transfusion, which has been proven to be effective in preventing strokes, silent cerebral infarcts, acute chest syndrome (ACS), and recurrent priapism, is a key treatment for acute and chronic complications of the disease and an effective intervention for decreasing morbidity and mortality in patients with SCD. It has been estimated that around 90% of all adults with SCD receive at least one transfusion in their lifetimes.[9] We found that only 12.9% of commercial and 17.3% of managed Medicaid SCD patients received outpatient blood transfusions in 2017. This varied by age, with patients ages 18 to 34 most likely to have received an outpatient transfusion (15.8% of commercial and 24.2% of managed Medicaid SCD patients), compared with

children under 18 (10.1% of commercial and 14.6% of managed Medicaid SCD patients) and patients ages 35 to 64 (13.2% of commercial and 12.5% of managed Medicaid SCD patients).

- **The direct medical cost of SCD patients is high.** SCD patients incurred annual medical and pharmacy costs that were several times greater than typical enrollees of similar age. For example, we report that an average commercial child with SCD incurred an average $2,715 per patient per month (PPPM) in 2017 and the average Medicaid child with SCD incurred an average $1,010 PPPM. To place these numbers into context, the average child in a commercial or managed Medicaid plan incurred around $250 per member per month (PMPM).[10,11] Commercial adults with SCD in our analysis incurred an average of $3,666 (ages 18-34) and $3,297 (ages 35+) PPPM as compared to a typical commercial adult member PMPM of $543. Adult managed Medicaid SCD patients incurred an average $2,864 (18-34) and $2,941 (35+) PPPM as compared to a $315 PMPM for a typical managed Medicaid member.[12] Inpatient admissions contributed a large portion to these expenditures (as much as 48% of the PPPM for commercial children) with SCD.

This report was commissioned by Global Blood Therapeutics, Inc. The findings and conclusions reflect the opinion of the authors; Milliman does not endorse any product or organization. If this report is reproduced, it should be reproduced in its entirety, as pieces taken out of context can be misleading. Our analysis is based on populations, practice patterns, and treatments present in the administrative claims databases specified in the Data Sources and Methodology section of this report. These factors may change over time, and findings from different populations and time periods may differ from the estimates presented in this report for many reasons.

As with any economic or actuarial analysis, it is not possible to capture all factors that may be significant. Further, no algorithms for identifying SCD or other medical or surgical conditions are perfect, and we relied only on the limited information available in claims data, without reference to medical records. Because we present national average data, the findings should be interpreted carefully before they are applied to any particular situation because there could be considerable variation among subsets of the population. One of the authors, Gabriela Dieguez, is a member of the American Academy of Actuaries and meets its qualification standards for this work.

BACKGROUND

SCD comprises a group of inherited red blood cell disorders that are caused by genetic mutations in beta globin (β-globin, *HBB* gene), the most common form of hemoglobin in humans.[13] The resulting structural abnormalities in hemoglobin cause hemolytic anemia and VOCs, which in turn lead to significant end-organ injury and premature death.[14] In the United States it is estimated that SCD affects approximately 100,000 people with the disease, occurring most often in African American (1 out of every 365 births) and Hispanic American (1 out of every 16,300 births) populations.[1] Although SCD is a congenital disease that leads to early death, most children in the United States and in other developed countries now survive into adulthood.[2] Improved survival among children in recent decades has shifted most of the morbidity and mortality associated with the disease to adulthood.[3] Because historically SCD has disproportionately affected individuals with a lower socioeconomic status, most adults and children with SCD rely on government-based health insurance programs, including Medicaid.[15] An earlier study published in 2005, for example, estimated that among African American children diagnosed with the disease, approximately 56.2% were publicly insured (with Medicaid or the Children's Health Insurance Program), 32.6% were privately insured, 4.1% were covered under another form of insurance, and 7.1% were uninsured.[16]

SYMPTOMS AND COMPLICATIONS

Symptoms and complications of SCD vary depending on the inheritance of specific mutations in the β-globin allele. For example, individuals with homozygous sickle cell anemia (characterized by the exclusive production of β-globin proteins HbSS and HbSβ^0) typically have shorter life expectancies and are at greater risk for central nervous system complications compared with individuals with compound heterozygous SCD, or sickle cell variant disease.[17] In all people with the disease, misshapen red blood cells and increased adhesion of blood cells lead to reduced blood flow, or vaso-occlusion, ischemia, and inflammation, which in turn lead to complications that typically are categorized as either acute or chronic.[18]

Acute complications of SCD include painful VOCs, ACS, and stroke.[19] VOCs, acute episodes of severe pain that often require hospitalization and the use of potent analgesics such as opioids, may begin during early childhood and typically recur throughout life.[20] ACS is one of the most common and serious acute complications associated with SCD, often occurring in patients hospitalized with VOCs and posing a high risk of SCD-related morbidity and mortality in children.[21] Stroke is also a common and significant complication of SCD that results in high morbidity and mortality in children and adults.[22,23] Without primary stroke prevention through transcranial Doppler (TCD) screening and chronic transfusions, approximately 10% of children with HbSS are likely to have overt strokes.[24]

In addition to stroke, another 20% to 35% of children with SCD have abnormalities on brain magnetic resonance imaging (MRI), which are thought to represent smaller, subclinical infarcts.[25] These silent cerebral infarcts (SCI) are frequently associated with cognitive impairment, an increased risk of further SCI or acute symptomatic stroke, and minor neurologic findings.[26] One multicenter study showed that lower baseline hemoglobin concentration and relatively high systolic blood pressure were risk factors for SCI in the SCD population.[27] Another study found that seizure history and a high white blood count were also associated with SCI risk in SCD patients.[28]

Longer-term complications of SCD include chronic injury of the kidneys and liver, as well as injury to the brain, eyes, heart, and lungs.[29] Most of these complications occur in response to a chronically compromised blood supply. Osteonecrosis is a common skeletal complication of SCD, where red cell sickling causes bone infarction that results in early onset degenerative arthritis, most frequently involving the femoral head.[30] Chronic hemolytic anemia, which occurs more commonly and increases in severity with age, also is a major contributor to organ dysfunction.[31] Approximately 4% to 18% of adults with SCD have deteriorating renal function that leads to advanced renal disease (stages 3 and 4).[32] Progressively restrictive lung function caused by fibrotic changes evident on computed tomography (CT) scans occurs in more than 70% of adults with SCD.[33] Evidence-based guidelines for the management of most of these complications are still unavailable and, therefore, current management is mostly consensus-based.[34,35]

DISEASE-MODIFYING TREATMENTS

To date, the only cure for SCD is a hematopoietic stem cell transplantation (HSCT). However, barriers preclude its widespread use including the availability of a matched donor, high mortality risk due to acute complications in the immediate post-transplant period, and longer-term problems of transplant rejection, poor end-organ function, and other adverse events.[36] However, there are two disease-modifying treatments that prevent and treat both the acute and chronic complications of SCD, specifically administration of HU and chronic blood transfusions.[37,38]

Treatment with HU significantly reduces the frequency of VOCs, ACS, and hospitalizations among individuals with SCD, and also results in the need for fewer blood transfusions and reductions in healthcare costs associated with the disease.[36] It raises the level of hemoglobin F and the overall hemoglobin level and decreases the rate of VOCs by 50%.[7] Moreover, HU treatment is associated with decreased mortality in symptomatic patients with SCD compared with patients receiving shorter-term HU or no HU.[6] In adults, the administration of HU lowers annual rates of pain crises, reduces the need for blood transfusions, and lowers the incidence of ACS.[39] The use of HU also results in lower costs from hospitalization among young patients with SCD.[40] In children, studies have shown that the use of HU results in sustained benefits with limited toxicity and limited adverse effects on growth and development.[41] However, there are patient, provider, and systems-level barriers to the effectiveness of HU in real-world clinical practice.[42] Adherence to treatment with HU is variable and overall is suboptimal.[8]

Chronic transfusion therapy is an important intervention in decreasing morbidity and mortality in patients with SCD, and transfusions are a key treatment for acute and chronic complications of the disease.[43] Chronic red blood cell transfusion is effective in the prevention of strokes, SCI, ACS, and recurrent priapism and in pregnancy to reduce maternal complications. Acute stroke is managed with red blood cell transfusion to reduce the percentage hemoglobin S level to below 30% to prevent progression of cerebral ischemia.[44] The optimal transfusion method to provide the best neurologic outcome is not clear. One multi-institutional retrospective study found that exchange transfusion was associated with a lower risk of subsequent stroke compared with simple transfusion at the time of stroke presentation.[45] Erythrocytapheresis (red cell exchange apheresis) is the most common type of blood transfusion used for initial treatment after a first stroke.[9] However, the benefits of transfusion therapy must be balanced with the inherent risks. Iron load among those receiving chronic transfusions is the most serious problem associated with transfusions. Iron overload is managed with iron chelation therapy to prevent hepatic, cardiac, and endocrinologic complications, and overall survival is increased if patients adhere to therapy that is instituted early.[46]

SUPPORTIVE THERAPIES

Improved survival among children in recent decades can be traced to diagnostic, prevention, and treatment strategies including newborn screening, penicillin prophylaxis, and vaccination against encapsulated organisms. Before these strategies were implemented, children with SCD commonly died of infection.[47] TCD screening to identify children at risk for stroke has allowed the use of transfusions to substantially reduce the risk of first stroke among children with the disease.[48] Folic acid supplementation is well established in the treatment of chronic hemolytic anemia.[49]

Pain, a major complication of SCD due to VOCs, is largely managed with opioid analgesics in the United States. According to clinical guidelines, opioids are recommended for treatment of acute pain episodes as well as chronic pain that cannot be otherwise managed, and many SCD patients require long-term opioid therapy to achieve adequate pain relief.[50] Opioid use in the SCD population is substantial and increases significantly when patients with SCD are transitioned to adult care. This pattern may reflect the chronic or accumulated damage from SCD that accumulates over time, resulting in significant end-organ damage and ischemic tissue injury.[46]

ACCESS TO SPECIALTY CARE

There is limited research on patient access to hematologist services and the effect on health outcomes, especially for children. For children, comprehensive care facilities can be staffed by pediatric hematologists, but care is often provided by family practitioners or pediatricians.[51] A recent study of commercial and Medicaid SCD patients of all ages from 2009 to 2014 indicated that a higher proportion of commercial SCD patients (39%-47%) saw a hematologist or oncologist than those in the Medicaid cohort (2%-15%).[52]

Given substantial improvements in the treatment of SCD in recent years, the average age of death has shifted from childhood to adulthood for patients with SCD.[2,3] Therefore, there is a growing emphasis on the transition from pediatric services to those provided in an adult healthcare setting. The age range for these “transitional years” varies between publications, but is generally from 18 to 22 years of age.[53] Other studies place less weight on a defined age range of transition, but focus on the importance of connecting services from childhood services to adult care.[54] A 2010 study found that the two years into the transition to adult care are a high-risk period for SCD patients, because of an imperfect link between services.[2] In addition, a multistate study of Medicaid patients with SCD showed that patients transitioning to adult care received fewer transfusions, HU treatment, and iron chelation therapy for iron overload, experienced greater healthcare costs, and had more frequent SCD-related complications compared to children.[55] We note that while we do not carve out the transitional population exclusively in our analysis, their experience is included in the analysis of the young adult (18 to 34 years) patient cohort.

UTILIZATION AND COSTS

Several prior studies have reported on the healthcare utilization and costs of SCD patients. An analysis of SCD-related emergency department (ED) visits and hospitalizations from eight geographically dispersed states in the 2005 and 2006 Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases and State Emergency Department Databases found that SCD patients had a mean of 1.5 hospitalizations and 1.1 ED visits per year. Utilization was highest for 18-year-olds to 30-year-olds and those with public insurance. The 30-day hospital readmission rate was also highest for these subgroups.[56] A 2005 study estimated that the total medical expenditures for children with SCD were $335 million dollars.[57] The same study found that children with SCD enrolled in Medicaid had lower mean expenditures than children with SCD enrolled in private insurance; however, expenditures from both payers increased with the patient's age. A study of Florida Medicaid-enrolled children and adults with SCD between 2001 and 2005 also found that healthcare costs generally rose with age and even non-SCD-related costs were significantly higher than the general population.[4] The researchers observed an increased rate of ED use in individuals greater than 19 years of age, and a high proportion of SCD-related costs associated with inpatient hospitalization. These studies confirmed that the total cost of SCD is substantial and comparable to other serious, chronic diseases, and SCD patients also experienced reduced quality of life, lost productivity, and premature mortality.

FINDINGS

For this analysis, we examined 2017 membership and administrative claims for all-cause healthcare expenditures. We reviewed a combination of the 2017 IBM Marketscan commercial data and Milliman's Consolidated Health Cost Guidelines Sources Database (CHSD) data for commercial enrollees in 2017. We also reviewed the CHSD's multistate data for managed Medicaid enrollees. Detailed descriptions of these data sources are provided in the Data Sources and Methodology section of this report. Figure 1 presents the sample size outcomes of the steps taken to identify 2017 SCD patient populations by payer type. After performing basic data quality screens, members were required to report qualified enrollment for all months of enrollment in 2017. For commercial mbmers, qualified coverage meant continuous medical and pharmacy coverage in a non-capitated health plan as an active employee (or dependent of one). For managed Medicaid members, qualified coverage required mostly continuous medical and pharmacy coverage for all months of enrollment in 2017 (allowing for a maximum of a one-month lapse in coverage per calendar year). Patients ages 65 and older as of the end of 2017 were excluded. Patients with qualified 2017 enrollment were required to report continuous qualified enrollment from January 2016 to December 2017 for patients ages 2 and older or from date of birth through the end of December 2017 for patients under age 2. SCD patients were identified among members meeting all of these requirements as those who reported a SCD diagnosis code on one acute inpatient or observation claim or two or more non-acute inpatient, ED, or outpatient evaluation and management claims on different dates of service. Detailed codes lists are provided in Figures 16 and 17 in the Data Source and Methodology section.

FIGURE 1: SELECTION OF ANALYSIS COHORT: PATIENTS WITH SCD IN 2017

	Commercial Population		Managed Medicaid*	
Data	**Members**	**% of Starting Population**	**Members**	**% of Starting Population**
Starting population	62,206,369	100%	5,108,294	100%
Data quality screens	60,382,085	97%	5,102,751	100%
Qualifying enrollment for all months enrolled in 2017	43,697,046	70%	5,094,012	100%
Age screen (patients < 65 years)	42,444,449	68%	4,888,473	96%
Full 2017 enrollment (12 months* or DOB to EOY) [1]	29,826,600	48%	2,871,084	56%
Full 2016 enrollment (12 months* or DOB to EOY)[1]	20,732,477	33%	2,090,886	41%
	SCD Patients		**SCD Patients**	
Study population	3,014		1,293	

*Full enrollment for managed Medicaid enrollees is defined as 11+ months (or DOB to EOY) within the calendar year.

[1] DOB = date of birth (applied for patients born in year); EOY = end of calendar year.

PREVALENCE AND DEMOGRAPHICS

We identified 3,014 commercially insured patients, yielding a prevalence rate of 18 per 100,000 commercial members. National estimates of SCD patient insurance are comprised of approximately 50% to 60% Medicaid members and 20% Medicare members, with a remainder of 20% to 30% commercial members.[58] Based on our calculated prevalence rate of 18 per 100,000 commercial members and available national enrollment information from the U.S. Census Bureau, we approximated roughly 31,000 commercial SCD patients in the United States, which is consistent with national estimates.[1,59] The Centers for Medicare and Medicaid Services (CMS) estimates approximately 55,000 Medicaid SCD patients across the United States.[39] CMS reports that there is wide variation of SCD prevalence across Medicaid states, with a range of prevalence rates of as low as .09 in West Virginia and as high as 2.20 per 1,000 Medicaid beneficiaries in Mississippi, based on analysis of claims from 2008 to 2012.[60] We identified 1,293 managed Medicaid-insured patients with SCD in 2017. Although the CHSD database is sufficiently robust to identify a representative study population of Medicaid SCD patients, we are not able to calculate a national prevalence estimate due to regional variability that is not represented in our data.

The transition of young adults with SCD from pediatric to adult medical care is important, given medical advances that have transformed SCD into a lifelong chronic condition, rather than a disease of childhood.[2] There is increased morbidity and mortality after the transition of adolescents and young adults with SCD to adult care. Therefore, we stratified the SCD patient populations into three age groups: under 18, 18 to 34, and 35 to 64 (Figure 2). The managed Medicaid patient cohort contained more children proportionately than the commercial population (41% vs. 34%, respectively).

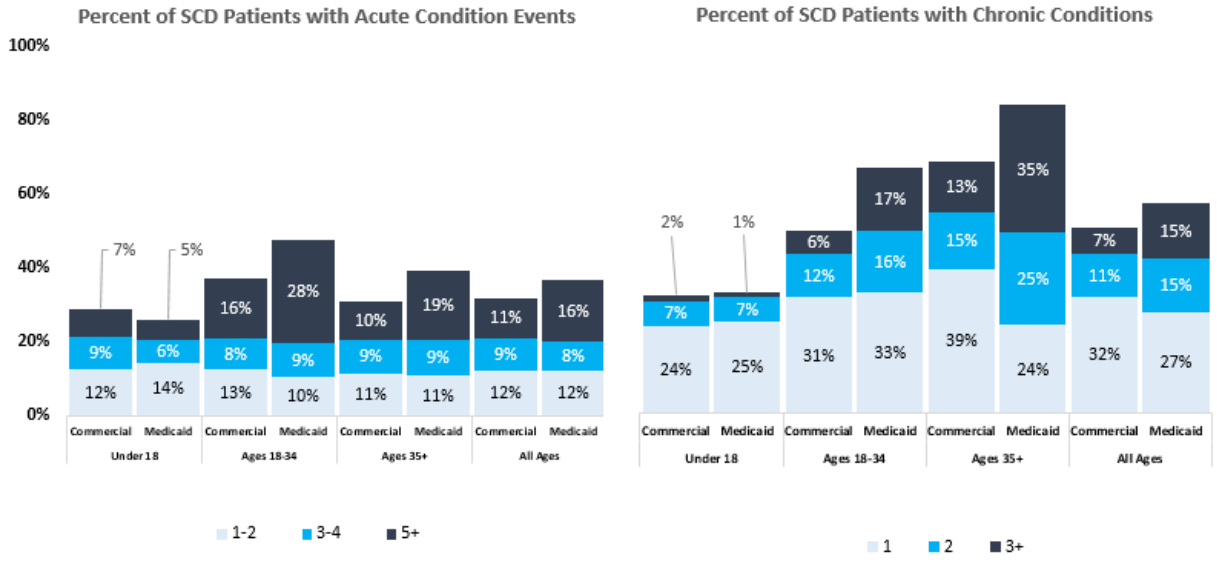
FIGURE 2: FREQUENCY OF ACUTE CONDITION EVENTS AND CHRONIC CONDITIONS BY PAYER AND AGE

	Patient Counts		Percentage of Population	
Age Group	**Commercial**	**Medicaid**	**Commercial**	**Medicaid**
Under 18	1,034	529	34%	41%
Ages 18-34	853	443	28%	34%
Ages 35+	1,127	321	37%	25%
Total	**3,014**	**1,293**	**100%**	**100%**

SCD-RELATED ACUTE EVENTS AND CHRONIC CONDITIONS

SCD patients may experience a number of associated acute conditions requiring hospitalization and develop chronic conditions from the effects of SCD. Hospitalizations for the following acute conditions were identified in claims data: acute kidney failure, acute cholecystitis/cholangitis, acute myocardial infarction, pneumonia, sepsis, splenic sequestration, stroke, and unspecified SCD crisis. Each hospitalization represented an acute condition event and more than one acute condition event was attributed to a single hospitalization if the patient had more than one acute condition during that hospital stay. Similarly, we identified SCD patients with the following chronic conditions: asthma, blindness or low vision, chronic kidney disease, chronic obstructive pulmonary disease (COPD), cognitive impairment, end-stage renal disease (ESRD), gallstones, heart failure, non-pressure ulcers of the lower extremity, osteonecrosis, pulmonary hypertension, retinopathy, and risk factors for SCI. Direct identification of SCI was not possible in administrative claims data because SCI is typically not overtly symptomatic but rather identified by MRI findings, which are not reported on claims. For the chronic condition termed “risk factors for SCI,” we assigned this condition when we observed a patient with hypertension, epilepsy, leukocytosis, or vascular leukoencephalopathy based on published literature that has demonstrated these conditions are SCI risk factors.[27,28] In Figure 3, we identify the percentage of SCD patients in the different age groups who had one or more of these conditions in 2017. While little difference by payer type was found among children, adult managed Medicaid SCD patients experienced more acute event hospitalizations as well as accumulated more chronic conditions than commercial patients.

FIGURE 3: FREQUENCY OF ACUTE CONDITION EVENTS AND CHRONIC CONDITIONS BY PAYER AND AGE



Overall, despite being a younger population on average (Figure 2 above), the managed Medicaid patient population presented as sicker, with a higher frequency of acute condition-related hospitalizations and number of chronic conditions.

We found that 32% of commercial and 37% of managed Medicaid SCD patients reported one or more hospitalizations associated with an acute condition in 2017. Across both payers, patients ages 18 or older were more likely than children to report such events. Figure 4 provides a distribution of the most common acute conditions. Our overall findings were consistent with the results of a nationwide study conducted by the Agency for Healthcare Research and Quality (AHRQ) that determined that about two-thirds of hospitalizations incurred by SCD patients in 2004 were for patients ages 18 to 44.[15]

FIGURE 4: FREQUENCY OF SCD PATIENTS WITH 1+ ACUTE CONDITION EVENTS BY PAYER

Commercial
Percentage of Acute Condition Events
Among the 32% of SCD Patients With 1+ Events

	<18	18-34	35+
Unspecified SCD Crisis	77%	93%	80%
Pneumonia	19%	29%	30%
Acute Chest Syndrome	32%	25%	19%
Sepsis	5%	12%	18%
Acute Kidney Failure	-	6%	21%
Splenic Sequestration	7%	-	-
Stroke	-	-	5%

Medicaid
Percentage of Acute Condition Events
Among the 37% of SCD Patients With 1+ Events

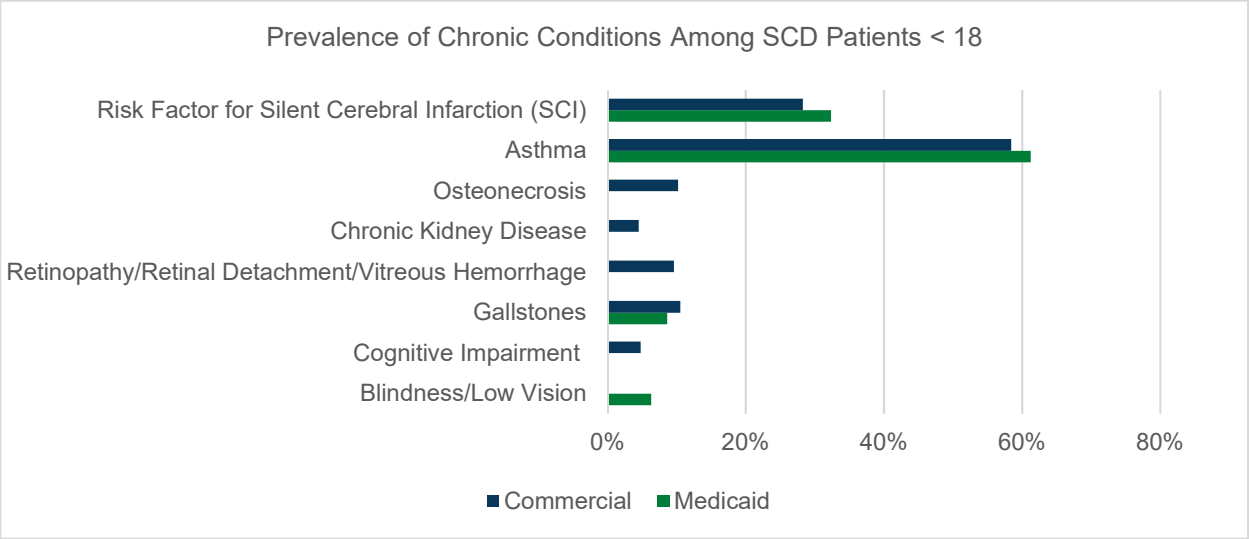
	<18	18-34	35+
Unspecified SCD Crisis	67%	92%	72%
Pneumonia	25%	32%	36%
Acute Chest Syndrome	31%	23%	13%
Sepsis	-	16%	22%
Acute Kidney Failure	-	11%	40%
Splenic Sequestration	8%	-	-

Note: The figure above illustrates the percentage of individual acute condition events for SCD patients who experienced one or more events leading to hospitalization by payer type. Frequencies do not sum to 100% as SCD patients with one or more events may have multiple acute condition events during the same or different hospitalizations in the year. Percentages for acute condition events with fewer than 11 patients are not reported and are indicated with a dash.

SCD patients ages 18 to 34 had the highest percentage of hospitalizations for an acute condition that included an unspecified SCD crisis event (VOCs not identified with diagnosis codes for splenic sequestration or ACS). The percentage of hospitalizations in a year for pneumonia, sepsis, and acute kidney failure increased with age for SCD patients across payers. Among hospitalizations for acute conditions, ACS events were more common for children under 18 than for adults.

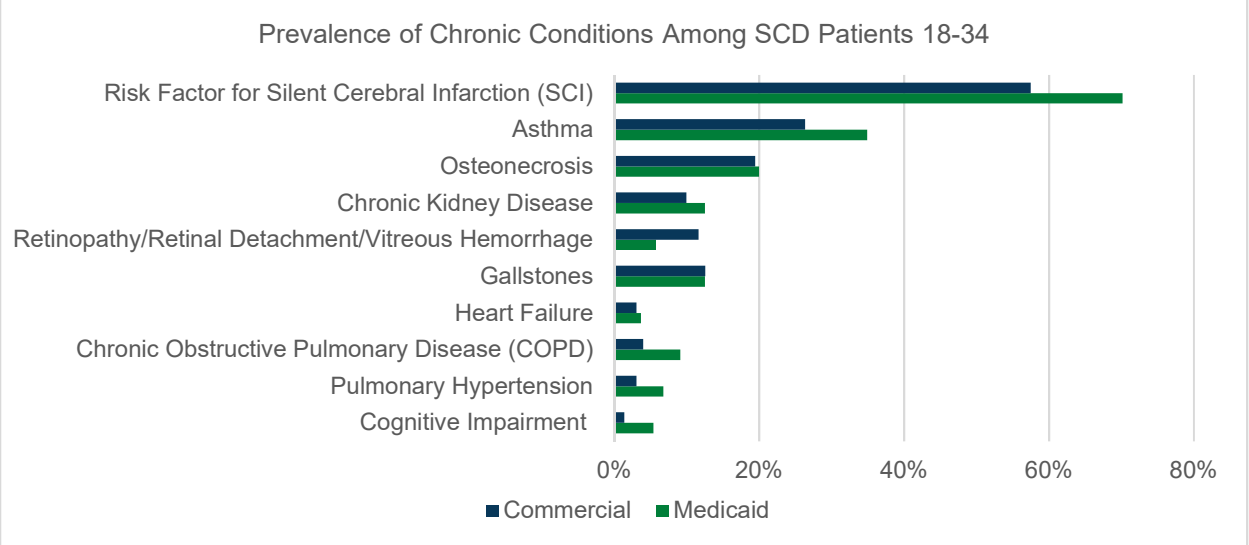
As Figure 3 above demonstrates, the number of chronic conditions increased with age. Figures 5 to 7 detail the most prevalent chronic conditions among SCD patients by age group. Asthma was the most common chronic condition for SCD patients under 18, reported for approximately 60% of SCD children. By comparison, an analysis of asthma data from the 2001-2016 National Health Interview Survey for children ages up to 17 determined that the overall prevalence of asthma was 15.7% for non-Hispanic black children.[61] Moreover, a majority of SCD patients 18 to 34 had a risk factor for SCI. Medicaid SCD patients were more likely than commercial patients to have chronic conditions in the 18-34 age group with the exception of retinopathy/retinal detachment/vitreous hemorrhage and gallstones. Commercial and managed Medicaid SCD patients 35 and older had the highest prevalence of a risk factor for SCI of any age group.

FIGURE 5: FREQUENCY OF SCD PATIENTS UNDER 18 WITH 1+ CHRONIC CONDITIONS BY PAYER



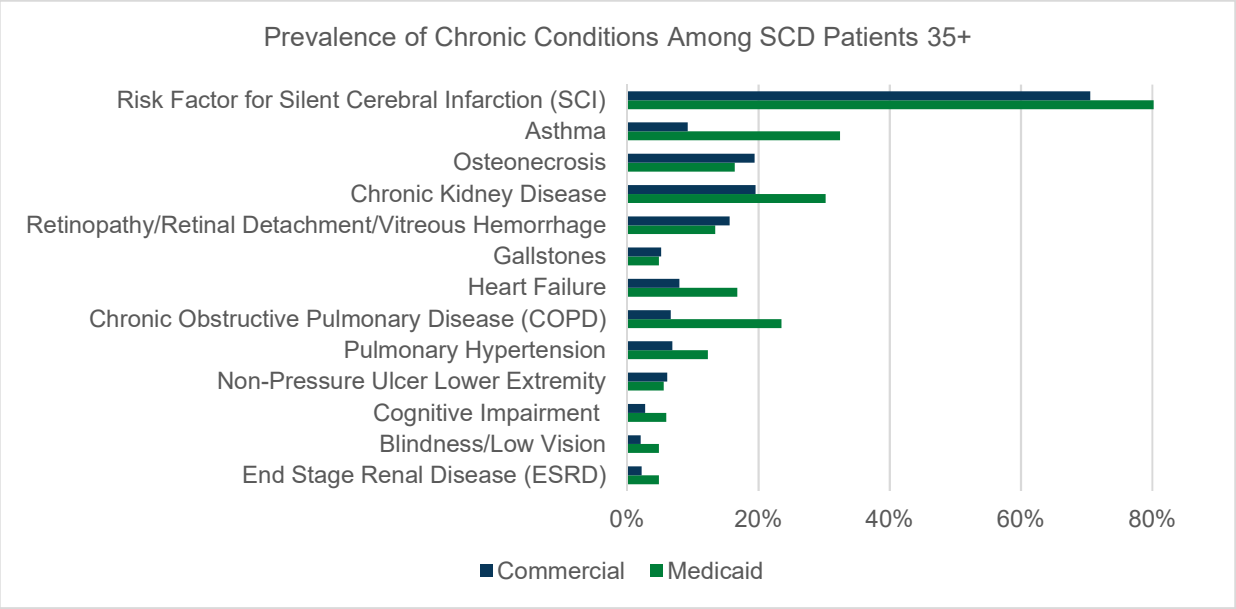
Note: Percentages for chronic conditions with fewer than 11 patients are not reported. Percentages of commercial and Medicaid SCD patients with ESRD, non-pressure ulcer lower extremity, COPD, and heart failure had sample sizes under 11 and were not included in the figure above. Commercial patients with blindness or low vision and Medicaid patients with osteonecrosis, chronic kidney disease, Retinopathy/Retinal Detachment/Vitreous Hemorrhage diagnoses, and cognitive impairment could not be reported.

FIGURE 6: FREQUENCY OF SCD PATIENTS AGES 18-34 WITH 1+ CHRONIC CONDITIONS BY PAYER



Note: Percentages for chronic condition events with fewer than 11 patients are not reported. Percentages of commercial and Medicaid SCD patients with ESRD and blindness or low vision had sample sizes under 11 and were not included in the figure above.

FIGURE 7: FREQUENCY OF SCD PATIENTS AGES 35-64 WITH 1+ CHRONIC CONDITIONS BY PAYER



Utilization of disease-modifying therapies

Two disease-modifying treatments that prevent and treat both the acute and chronic complications associated with SCD are administration of HU and repeated long-term blood transfusions.[62,38] Transfusion therapy is an important intervention in decreasing morbidity and mortality in patients with SCD, and transfusions are a key treatment for acute and chronic complications of the disease.[63] Iron overload associated with these transfusions is managed with iron chelation therapy to prevent hepatic, cardiac, and endocrinologic complications.[64] Figure 8 reports the observed rate of patients with one or more outpatient transfusions incurred by SCD patients in 2017.

FIGURE 8: ANNUAL OUTPATIENT BLOOD TRANSFUSION AND IRON CHELATION THERAPY UTILIZATON AMONG SCD PATIENTS WITH 1+ OUTPATIENT BLOOD TRANSFUSIONS IN 2017

	Commercial All Ages	Medicaid All Ages
Outpatient Blood Transfusions	**12.9%**	**17.3%**
Simple Red Cell	11.4%	15.1%
Red Cell Exchange Transfusion	0.6%	2.5%
Red Cell Exchange Apheresis	3.2%	3.9%
Average number of transfusions for patients with 1+ transfusion	*5.8*	*6.4*
Percent of patients with 1+ transfusion who receive iron chelation	28.4%	41.1%
Average iron chelation days supply for patients with 1+ transfusion who receive iron chelation	*169.0*	*198.4*

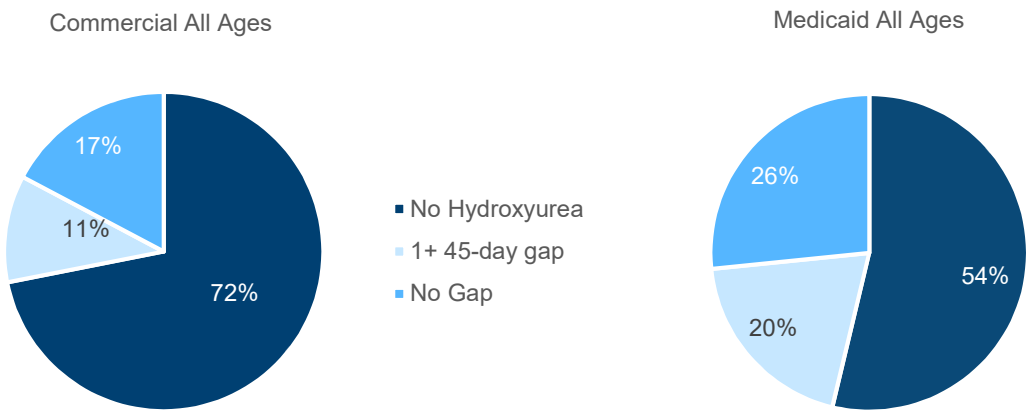
We observed that 12.9% of commercial and 17.3% of managed Medicaid SCD patients received outpatient blood transfusions. This varied by age, with patients ages 18 to 34 most likely to receive an outpatient transfusion (15.8% of commercial and 24.2% of managed Medicaid SCD patients) as compared to children under 18 (10.1% of commercial and 14.6% of managed Medicaid SCD patients) and patients ages 35 to 64 (13.2% of commercial and 12.5% of

managed Medicaid SCD patients). The most common outpatient blood transfusion type was simple red cell transfusion. Managed Medicaid SCD patients received more outpatient transfusions on average than commercial SCD patients among patients who received at least one during the year.

We also observed that 41.1% of managed Medicaid SCD patients with outpatient blood transfusions received iron chelation therapy compared to 28.4% of commercial SCD patients. This varied by age, with the highest percentage of children under 18 with one or more transfusions receiving iron chelation therapy (39% for commercial and 57% for managed Medicaid). Managed Medicaid SCD patients with one or more transfusions who received iron chelation therapy had a higher average day's supply of iron chelation drugs than commercial SCD patients (198.4 compared to 169.0 days, respectively).

Multiple studies have found that HU treatment rates for patients with SCD are low and adherence is poor.[8,38] One cross-sectional study of SCD patients ages 18 to 22 in 2015 reported a particularly low rate of adherence to HU, with 74% of patients reporting little to no adherence.[42] A study of North Carolina Medicaid SCD patients reported an adherence rate of 35% among patients who received at least two prescriptions for HU in a review of claims from 2000 to 2008. Another study of 390 Maryland managed Medicaid SCD patients covered in 2001 to 2005 reported that a large majority (85.9%) did not refill a single prescription for HU.[65,66] Figure 9 provides details on how many SCD patients in our analysis population filled one or more prescriptions for this drug in 2017 and, among those who did, how many reported nonpersistent use of the drug. Consistent with at least one other study, we distinguished patients with nonpersistent utilization of HU as those patients with a gap in HU therapy for 45 or more days.[71] We recognize a limitation in calculating gaps in therapy because most prescription benefits allow maintenance medications to be refilled up to 25% early. This means that a 30-day prescription could be filled every 23 days, which could result in an accumulation of patient on-hand medication resulting in a false positive identification of a gap in therapy in future months. For this analysis, patients with only one prescription filled for HU were considered to have “No Gap.”

FIGURE 9: ANNUAL HU TREATMENT UTILZATION BY PAYER IN 2017



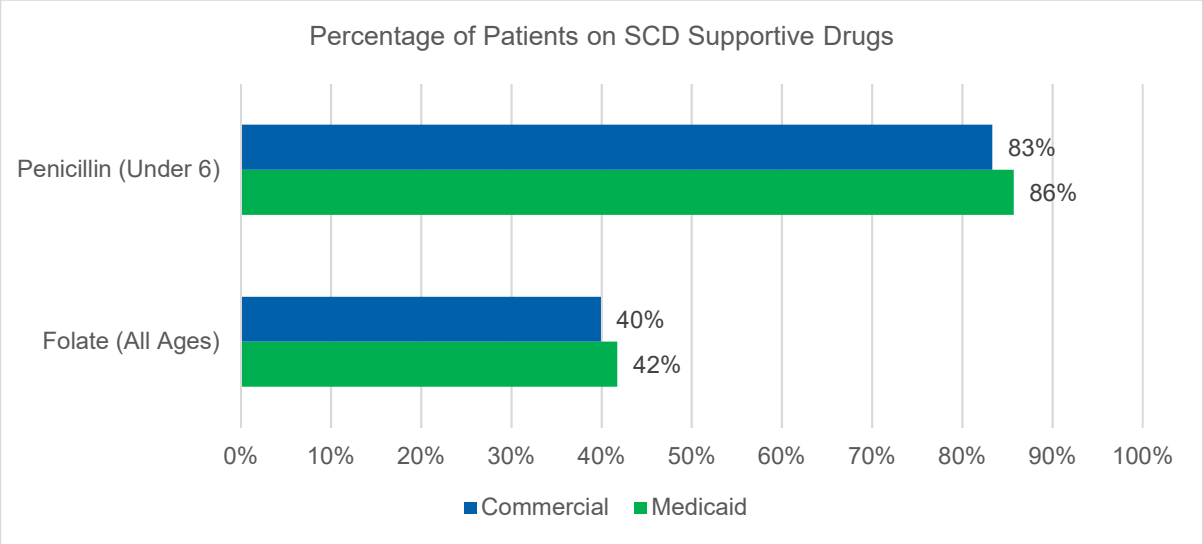
A higher percentage of managed Medicaid SCD patients (46%) than commercial SCD patients (28%) filled at least one prescription for HU. A substantial portion of SCD patients who filled a prescription for HU experienced at least one gap of 45 or more days in treatment across both payers (39% of commercial SCD patients and 43% of managed Medicaid SCD patients).

Utilization of supportive drugs

SCD patients may be treated with several other supportive drugs. Figure 10 details the rate of utilization (as measured by one or more prescription fills) of penicillin and folic acid (folate) for patients ages 5 and under. Most children with SCD age 5 and under filled prescriptions for penicillin in a year, consistent with clinical guidelines that

recommend universal penicillin prophylaxis for SCD patients in this age range.[49] About 40% of SCD patients filled a prescription for folate in a year. Although it has been suggested that folate in anemia raises hemoglobin levels and helps provide a healthy reticulocyte response, the use of folic acid in patients with SCD is not well supported by the literature and a recent review found there is little evidence to support or refute the practice of folate supplementation in people with SCD. Our findings on folate suggest the practice of prescribing the drug to SCD patients is variable across these patients and is not related to payer.[67] We note that folic acid is available in over-the-counter forms and total utilization of this therapy might be underreported as a result.

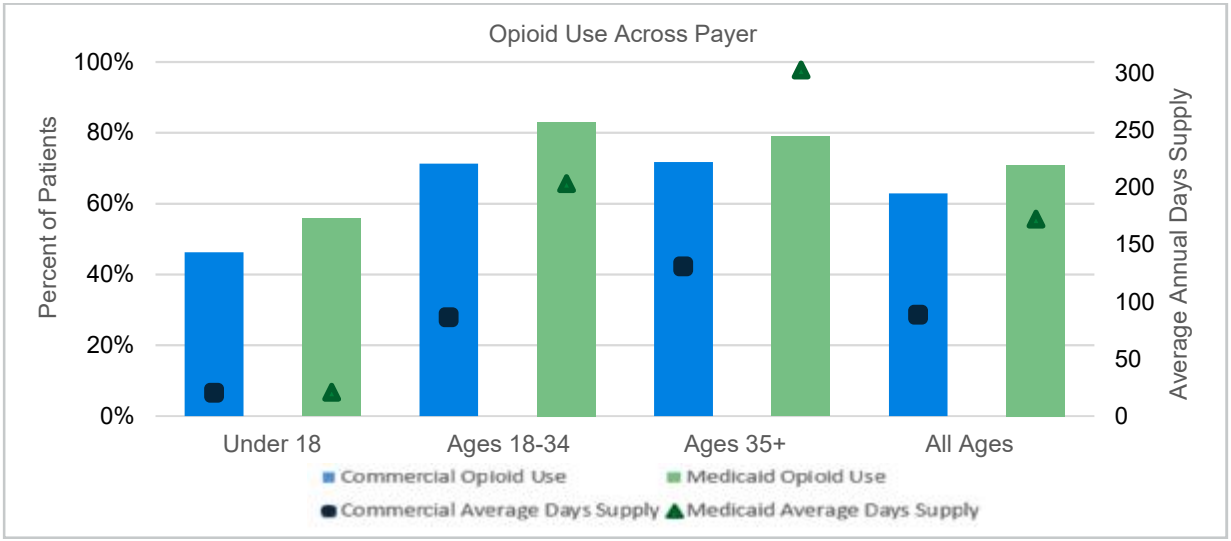
FIGURE 10: ANNUAL UTILIZATION OF SUPPORTIVE DRUGS BY SCD PATIENTS BY PAYER IN 2017



Pain management

Pain management is an important component of an SCD patient's treatment, both for acute conditions such as VOCs and chronic conditions like osteonecrosis that typically accrue and worsen with age. Figure 11 reports the average 2017 annual rate of all-cause opioid use, along with the average days supplied for SCD patients by payer and age.

FIGURE 11: ANNUAL SCD PATIENT UTILIZATION OF OPIOIDS BY PAYER AND AGE IN 2017



* Opioid use indicates a least one medical claim or prescription filled for an opioid drug.

Over 70% of commercial SCD patients and approximately 80% of managed Medicaid SCD patients over the age of 18 had at least one medical claim or prescription filled for an opioid drug. We observed a higher rate of opioid use among adults than children for both payers. Opioid use, measured by days supply across all drug claims reported for those who had at least one outpatient opioid administration or prescription fill, increased with age, although the percentage of patients with at least one administration or fill remained consistent throughout the adult age groups. This measure does not account for overlap of administration between acute and long-acting opioid drugs. Commercial SCD patients 35 years or older had outpatient opioid administration or filled scripts that covered 131 days out of the year, compared to 303 days for managed Medicaid SCD patients.

Access to care

While adequate and prompt management of the acute complications of SCD remains a mainstay of clinical care, access and coordination of care throughout the life span, including among primary care practitioners (PCPs), hematologists, and other specialists, can improve patients' health and well-being.[68] Timely and appropriate treatment of acute illness is critical, because life-threatening complications develop rapidly.[69] In addition, comprehensive, coordinated care is important for the management of chronic pain and chronic conditions that result from the SCD disease process. Guideline-recommended care includes the use of blood transfusions and routine use of HU to reduce the incidence of VOCs and ACS, and reduce mortality.[70] Hematologists play an important role in providing and monitoring response to these treatments in the outpatient setting.

We summarize the number of patients with at least one outpatient (OP) office visit (as measured by count of distinct dates of service reporting outpatient evaluation and management services) billed by either a PCP or hematologist (Figure 12). We focused on outpatient visits due to our interest in determining whether SCD patients had access to nonurgent, potentially ongoing hematologist care, as opposed to urgent hematologist care in the ED or during an inpatient hospitalization that would not represent hematologist management over time.

FIGURE 12: PERCENT OF PATIENTS WITH ONE OR MORE OUTPATIENT VISITS TO PCPS AND HEMATOLOGISTS IN 2017 BY PAYER AND AGE

		% of Patients With OP Visits	% of Patients With 1+ PCP Visit	% of Patients With 1+ Hematology Visit
Commercial	**1: Under 18**	95%	88%	50%
	2: Ages 18-34	88%	79%	28%
	3: Ages 35+	90%	85%	28%
	All Ages	**91%**	**85%**	**35%**
Managed Medicaid	**1: Under 18**	92%	82%	51%
	2: Ages 18-34	89%	81%	39%
	3: Ages 35+	87%	83%	29%
	All Ages	**90%**	**82%**	**41%**

In Figure 12, we show that only 35% of commercial SCD patients and 41% of managed Medicaid SCD patients had an outpatient hematology visit during 2017. Hematologist utilization varied by age and payer type, with a substantially higher percentage of children than adults having an outpatient hematologist visit. A higher utilization rate of at least one hematologist visit was observed in managed Medicaid patients ages 18 to 34 (39%) compared to the commercially insured 18 to 34 patient population (28%), an expected finding because the managed Medicaid patients

in this age group reported a higher number of acute condition hospitalizations and level of chronic condition accumulation (see Figure 3).

FIGURE 13: AVERAGE ANNUAL NUMBER OF OUTPATIENT PCP AND HEMATOLOGY SPECIALIST VISITS IN 2017 BY PAYER AND AGE

		Patients with 1+ OP Hematology Visit & 1+ PCP Visit			Patients with PCP Visit Only
		PCP	Outpatient Hematology	Total	PCP
Commercial	1: Under 18	3.9	3.6	7.6	4.9
	2: Ages 18-34	4.2	4.7	9	4.4
	3: Ages 35+	4.9	4.7	9.6	4.9
	All Ages	**4.3**	**4.2**	**8.5**	**4.8**
Managed Medicaid	1: Under 18	4.4	3.7	8.1	4.1
	2: Ages 18-34	6.7	5	11.7	5.9
	3: Ages 35+	6.8	4.7	11.5	6.1
	All Ages	**5.6**	**4.3**	**9.9**	**5.4**

In Figure 13, we compare the average number of visits for those patients reporting outpatient visits with both a PCP and a hematologist to those with just a PCP visits in the year. Patients who saw both a PCP and hematologist reported a similar or slightly higher number of PCP visits as those who saw a PCP alone, and reported around twice the number of total outpatient visits. This finding suggests that patients seeking specialist care are doing so in addition to, and not in place of, their PCP care. SCD patients ages 35 and older had the highest average number of PCP and hematologist visits across payers. This is consistent with the significant burden of chronic conditions observed in this age band of SCD patients. In addition, the number of outpatient hematologist visits was similar for commercial and managed Medicaid SCD patients who saw both a PCP and a hematologist. This suggests that access to ongoing outpatient hematology care for these patients was unrelated to payer type.

COSTS AND UTILIZATION

SCD patients, on average, are costly due to associated acute and chronic conditions that result in costly interactions with the healthcare system. Figure 14 provides average annual healthcare service utilization rates, as measured in terms of per 1,000 SCD patients. Compared to a 2009 study of Florida Medicaid patients, we found lower rates of inpatient admissions among managed Medicaid SCD patients, particularly in children.[4] In 2017, we found an average of 604 inpatient admissions per 1,000 managed Medicaid children (across multiple states) as compared to 1,231 in that prior study. Similarly, Florida Medicaid SCD adults in the 2009 study reported an average 2,338 inpatient admissions per 1,000 adults, and in our 2017 analysis we found an average of 1,964 inpatient admissions per 1,000 managed Medicaid adults.

In contrast, we observed higher utilization of ED visits among managed Medicaid SCD patients than the 2009 Florida Medicaid study. In that study, managed Medicaid children reported an average number of ED visits of 975 per 1,000 children. In 2017, we found an average of 1,334 ED visits per 1,000 managed Medicaid children. It is possible that, in the current healthcare environment, patients with SCD presenting with symptoms to the hospital are more likely to be managed in the ED and discharged without admission. Under such a scenario, less costly ED care would be substituting for certain inpatient hospitalizations that would have occurred a decade ago.

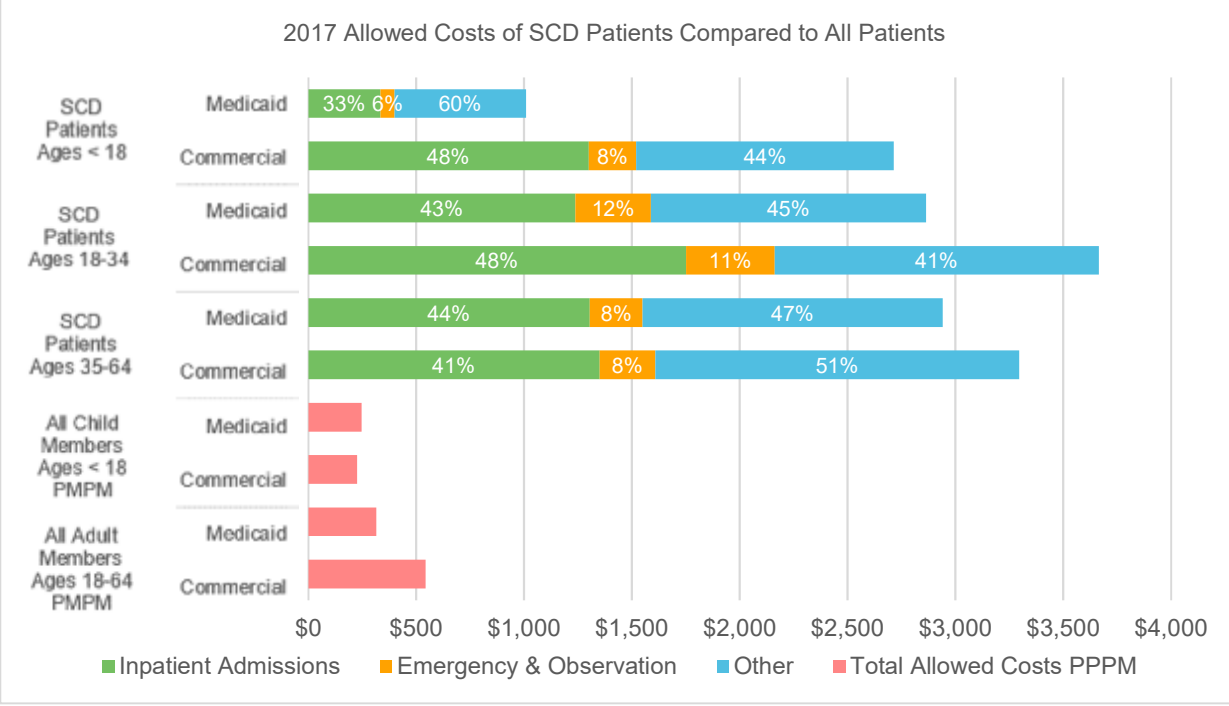
FIGURE 14: AVERAGE ANNUAL UTILIZATION OF ACUTE HEALTHCARE SERVICES AMONG SCD PATIENTS

Services	Utilization/Per 1,000 SCD Patients per Year					
	SCD Patients Ages < 18		SCD Patients Ages 18-34		SCD Patients Ages 35-64	
	Commercial	Medicaid	Commercial	Medicaid	Commercial	Medicaid
Inpatient Admissions	686	604	1,101	2,167	747	1,683
Emergency Dept.	1,036	1,344	2,014	6,871	1,083	4,546
Observation	93	116	234	636	161	472

Managed Medicaid SCD patients ages 18 and older had higher rates of ED visits, inpatient admissions, and observation services than commercial SCD patients, consistent with their reporting more acute condition events and chronic conditions (see Figure 3). Commercial SCD patients under the age of 18 had slightly higher utilization of inpatient admissions than managed Medicaid SCD patients in the same age group. Consistent with a prior study of 2013-2014 healthcare service utilization of commercial and Medicaid SCD patients, we found that managed Medicaid SCD patients reported more ED utilization than commercial patients.[61] Rates of ED visits and observation stays were highest among SCD patients ages 18 to 34.

Figure 15 presents the average allowed costs (amounts paid by both patient and payer combined) incurred per SCD patient per month (PPPM). Additionally, the commercial and managed Medicaid member allowed costs (in terms of per member per month or PMPM) for the average member (across all enrollees) are provided for context. SCD patient spending in both managed Medicaid and commercial plans varies by factors such as locale and eligibility. We have not adjusted for these variables.

FIGURE 15: MONTHLY ALLOWED SPENDING (PPPM) BY SCD PATIENT AGE GROUP



Notes:
Commercial average allowed PMPM derived from available fiscal year 2017 data using Milliman Managed Care Rating Model 2017.[13]
Medicaid average allowed PMPM derived from available fiscal year 2014 data as reported by KFF, assuming zero trend.[12,14]
Other represents all medical and pharmacy claims other than inpatient admissions, emergency room services, and observation visits.

A 2009 study of Florida Medicaid SCD patients found average costs on a PPPM basis were $1,041 for children 19 and younger and $2,188 for adults 20 to 65.[4] For managed Medicaid SCD patients, we found a nationwide average 2017 PPPM of $1,010 for children under 18 and $2,896 for ages 18 and older in allowed spending. While the pediatric averages are quite similar between the prior report and this analysis, we note that our analysis reflects multiple states of managed Medicaid (not just Florida and excluding fee-for-service Medicaid patients). Furthermore, changes in treatment patterns, including a shift from inpatient admissions to ED visits previously discussed in the context of Figure 14 above, likely contributed to children actually costing less on a constant dollar basis a decade later. For commercial SCD patients, allowed spending PPPMs were three times higher than managed Medicaid values, with children under 18 incurring an average PPPM of $2,715 and adults 18 to 64 around $3,455.

In the adult population, spending for inpatient hospitalizations accounted for 41% to 48% of the allowed costs PPPM, with ED visits and observation stays comprising another 8% to 12%. The high contribution of inpatient spending is consistent with the high rate of acute condition events requiring hospitalization reported in Figure 3. Despite managed Medicaid patients reporting more acute conditions requiring hospitalization, managed Medicaid SCD patients cost less than commercial patients. We suspect that this is largely driven by the more generous fee schedules found among commercial plans.

IMPLICATIONS FOR PAYERS

The analysis of real-world SCD patients can provide insights to commercial and managed Medicaid payers about the resource utilization and cost burden of this population and can point to challenges in managing this condition. Higher survival rates among children with SCD into adulthood have shaped the current payer economic burden of SCD. Organ damage accumulates over time, affecting the morbidity and healthcare needs of SCD patients as they age.

Our claims analysis of SCD patients reveals that:

- **The cost burden of sickle cell disease (SCD) is high:** SCD patients incurred, on average, $3,206 and $2,126 per month in combined medical and prescription drug expenses for commercial and managed Medicaid payers, respectively, in 2017. About half of that spending was related to inpatient services and ED visits (55% among commercial and 53% among managed Medicaid SCD patients).
- **Chronic conditions accumulate quickly as patients move through early adulthood**: The percentage of SCD patients with three or more chronic conditions doubled from ages 18-34 to ages 35-64 (from 6% to 13% among commercial and from 17% to 34% among managed Medicaid SCD patients).
- **Access to hematology care is a challenge**: A majority of patients in our study (65% of commercial and 59% of managed Medicaid SCD patients) did not incur a single outpatient hematology visit in 2017.
- **Adherence to existing treatments to manage or reduce acute and chronic conditions is poor:** While HU has been proven effective in reducing the frequency of pain episodes, only 28% of commercial and 46% of managed Medicaid SCD patients in our study filled at least one prescription for the drug, and gaps in treatment were very common (40% among commercial and 43% among managed Medicaid SCD patients). Furthermore, only a fraction of the patients in our study received blood transfusions in 2017 (13% of commercial and 17% of managed Medicaid SCD patients), despite transfusions being key for treatment of acute and chronic complications,.

These findings point to several unique opportunities and challenges for payers around the management of SCD patients, including the cost of acute events, the unique challenges of the transition years and young adulthood (ages 19-34 years), and the barriers to treatment faced by real-world patients with commercial and managed Medicaid coverage.

DATA SOURCES AND METHODOLOGY

DATA SOURCES

IBM MarketScan®

This is an annual medical database that includes geographically diverse, private sector health data from approximately 100 payers. The data set contains more than 28 million commercially insured lives. It represents the medical experience of insured employers and their dependents for active employees, early retirees, COBRA continues, and Medicare-eligible retirees with employer-provided Medicare Supplemental plans. The data set consists of person-specific clinical utilization, expenditures, and enrollment across inpatient, outpatient, prescription drug, and carve-out services from a selection of large employers, health plans, and governmental and public organizations. The MarketScan database links paid claims and encounter data to detailed patient information across sites and types of providers over time. This data set provided utilization and costs for the commercial population. We used data years 2016 and 2017 for this analysis. To be eligible for analysis, members were required to report continuous medical and pharmacy enrollment in a non-capitated health plan from January 2016 or, if born in 2016 or 2017, from date of birth, through the end of 2017. Members ages 65 or older as of December 2017 were excluded.

Milliman Consolidated Health Cost Guidelines™ Sources Database (CHSD)

The CHSD contains proprietary historical claims experience from several of Milliman's Health Cost Guidelines (HCG) data contributors. The database contains annual enrollment and paid medical and pharmacy claims for over 30 million commercially insured individuals covered by the benefit plans of large employers, health plans, and governmental and public organizations nationwide. Other groups included in the database are COBRA, Medicare Supplemental, and managed Medicaid. Managed Medicaid data includes medical and pharmacy claims for over 6 million managed lives and allows for multistate analyses (but is limited to several states). This data set provided utilization and costs for the managed Medicaid and commercial populations. We used data years 2016 and 2017 for this analysis. To be eligible for analysis, members were required to report semi-continuous medical and pharmacy enrollment from January 2016 or, if born in 2016 or 2017, from date of birth, through the end of 2017. Due to the amount of churn of member enrolling and disenrolling, we allowed members to report no more than a one-month gap in coverage per calendar year. Members ages 65 or older as of December 2017 were excluded.

The majority of this analysis assessed utilization and costs in 2017. However, 2016 claims were required to assess annual drug adherence rates.

METHODOLOGY

Identification of 2017 prevalent sickle cell disease patient population

For these analyses, we identified all patients diagnosed with SCD in 2017. SCD patients were required to report a sickle cell disease ICD-10-CM diagnosis code in any position on at least one acute inpatient or observation claim or at least two emergency department, non-acute inpatient, or outpatient claims on different dates of services. Figure 16 provides the list of SCD diagnosis codes and Figure 17 provides the Healthcare Common Procedure Coding System (HCPCS) and revenue codes used to identify the qualified claim types used in this identification algorithm. With this methodology, we identified 3,014 commercial and 1,293 managed Medicaid SCD patients.

The CHSD database provided the data for managed Medicaid and contributed to the commercial patient populations. While this data source is robust at a national level, the underlying data is unevenly distributed across states. For a disease such as SCD, which has higher incidence rates among the African American population, lacking data for key regions with a disproportionate share of these members will cause prevalence rates to be biased. As such, we used Marketscan alone to determine the commercial SCD prevalence rate and did not calculate an actual prevalence for managed Medicaid.

FIGURE 16: ICD-10-CM SCD DIAGNOSIS CODES

ICD-10-CM Code	Descriptor
D5700	Hb-SS disease with crisis, unspecified
D5701	Hb-SS disease with acute chest syndrome
D5702	Hb-SS disease with splenic sequestration
D571	Sickle-cell disease without crisis
D5720	Sickle-cell/Hb-C disease without crisis
D57211	Sickle-cell/Hb-C disease with acute chest syndrome
D57212	Sickle-cell/Hb-C disease with splenic sequestration
D57219	Sickle-cell/Hb-C disease with crisis, unspecified
D5740	Sickle-cell thalassemia without crisis
D57411	Sickle-cell thalassemia with acute chest syndrome
D57412	Sickle-cell thalassemia with splenic sequestration
D57419	Sickle-cell thalassemia with crisis, unspecified
D5780	Other sickle-cell disorders without crisis
D57811	Other sickle-cell disorders with acute chest syndrome
D57812	Other sickle-cell disorders with splenic sequestration
D57819	Other sickle-cell disorders with crisis, unspecified

FIGURE 17: QUALIFIED CLAIMS USED IN IDENTIFICATION OF SCD PATIENTS

Claim Type	CPT/HCPCS Code	Revenue Code
Outpatient	99201-99205, 99211-99215, 99241-99245, 99341-99345, 99347-99350, 99381-99387, 99391-99397, 99401-99404, 99411, 99412, 99429, 99455, 99456, G0402, G0438, G0439, G0463, G0466-G0468, T1015	0510-0517, 0519-0523, 0526-0529, 0982, 0983
Non-acute inpatient	99304-99310, 99315, 99316, 99318, 99324-99328, 99334-99337	0118, 0128, 0138, 0148, 0158, 0190-0194, 0199, 0524, 0525, 0550-0552, 0559
Acute inpatient	99221-99223, 99231-99233, 99238, 99239, 99251-99255, 99291, 99468, 99469, 99471,99472, 99475-99480	010x, 0110-0115, 0117, 0119-0125, 0127, 0129-0135, 0137, 0139-0145, 0147, 0149-0155, 0157, 0159-0160, 0164, 0166-0175, 0179, 0200-0204, 0206-0214, 0219, 0720-0722
Observation	99217-99220, 99224-99226, G0378, G0379	
Emergency department	99281-99285, G0380-G0384	0450-0452, 0456, 0459, 0981

Identification of acute condition events and chronic conditions

We identified SCD patients with specific chronic conditions in 2017. We examined diagnosis codes on all medical claims, excluding diagnostic laboratory and pathology claims and outpatient hospital and professional technical component claims for radiology services. The presence of at least one diagnosis code in any position on a claim identified the following chronic conditions: blindness or low vision, cognitive impairment, gallstones, non-pressure ulcers of a lower extremity, osteonecrosis, retinopathy or retinal detachment or vitreous hemorrhage, or risk factors for SCD including epilepsy, hypertension, elevated white blood count, or vascular leukoencephalopathy.

For chronic conditions for which patients are more likely to seek ongoing treatment, we examined diagnosis codes on qualified claims incurred in 2017. These conditions included asthma, chronic kidney disease, ESRD, COPD, heart failure, and pulmonary hypertension. A condition was identified if a diagnosis code for the condition was reported in any position on one acute inpatient claim, one observation claim, or two or more non-acute inpatient, emergency department, or outpatient qualified claims on different dates of service. (See Figure 17)

Similarly, we identified SCD patients with specific acute conditions requiring hospitalization in 2017. We examined diagnosis codes on acute inpatient hospital claims for SCD patients. Acute conditions were identified for each and every inpatient claim reporting the diagnosis code and a single admission was allowed to flag as many acute conditions as reported. Multiple instances of the same acute condition in the year were each counted as unique events. Metrics quantifying these events measured the number of inpatient admissions reporting a diagnosis code for each acute condition. The acute conditions analyzed included: ACS, acute cholecystitis/cholangitis, acute kidney failure, acute myocardial infarction, pneumonia, sepsis, splenic sequestration, stroke, thrombophlebitis, and unspecified SCD crises.

The ICD-10-CM diagnosis codes used in these algorithms are found in Appendix A. Events and conditions flagged for fewer than 11 patients were censored for this report.

Identification of blood transfusions

Transfusion days were identified on outpatient claims incurred in 2017 as days of service reporting a HCPCS or revenue code for a blood transfusion. Days of iron chelation were identified by either the number of days supplied reported on pharmacy claims for iron chelation drugs or for each day of service reporting an iron chelation HCPCS code. See Appendix B for the list of HCPCS and revenue codes and generic drug names used in this algorithm.

Drug utilization

We identified all physician or pharmacy administration claims for HU, glutamine, penicillin, folate, and opioids. While we reviewed claims for glutamine, we found little utilization of this drug. Refer to Appendix C for the complete list of generic drug names for these drugs. We used the reported days supplied on pharmacy claims. For medical drug claims, each reported HCPCS code was considered a one-day supply with the exception of J0570, an opioid, which counted as a 180-day supply.

We measured nonpersistence of HU utilization in this analysis. Among patients who received HU in 2017, we identified the subset of patients who reported continuous enrollment throughout 2016 to use in the measurement of nonpersistence. We then reviewed HU prescription fills and flagged gaps between prescriptions. We identified those patients with at least one gapp of at least 45 days, not counting days of inpatient admission, between the last date covered by a prior prescription and the next prescription fill date. This is consistent with the methodology used in am HU adherence study from 2018.[71]

Summary of costs

Costs reported in these analyses represent total allowed amounts, the amounts paid to providers by both payer and patient combined, reported on medical and pharmacy claims. Average costs are reported as average allowed amounts per SCD patient per month (PPPM).

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