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Survival of children with sickle cell disease

Charles T. Quinn, Zora R. Rogers, and George R. Buchanan

From the Division of Hematology-Oncology, Department of Pediatrics, University of Texas Southwestern Medical Center at Dallas, and Center for Cancer and Blood Disorders, Children's Medical Center Dallas, Dallas, TX.

Abstract

Contemporary survival data are not available for children with sickle cell disease (SCD). The few previous childhood SCD cohort studies do not reflect the benefits of modern therapy. We defined an inception cohort of newborns with sickle cell anemia (SS), sickle- β^0 -thalassemia ($S\beta^0$), sickle-hemoglobin C disease (SC), or sickle- β^0 -thalassemia ($S\beta^0$) who were identified by newborn screening and followed for up to 18 years. The incidence of death and stroke were calculated. Overall survival, SCD-related survival (considering only SCD-related deaths), and stroke-free survival were determined. The 711 subjects provided 5648 patient-years of observation. Twenty-five subjects died; mean age at death was 5.6 years. Five patients died from infection. Thirty had at least one stroke. Among SS and $S\beta^0$ subjects ($n = 448$), the overall rates of death and stroke were 0.59 and 0.85/100 patient-years. Survival analysis of SS and $S\beta^0$ subjects predicted the cumulative overall, SCD-related, and stroke-free survival to be 85.6%, 93.6%, and 88.5% by 18 years of age. No SCD-related deaths or strokes occurred in SC or $S\beta^+$ subjects ($n = 263$). Childhood mortality from SCD is decreasing, the mean age at death is increasing, and a smaller proportion of deaths are from infection.

Introduction

Sickle hemoglobin (Hgb S) causes a group of related blood disorders called sickle cell disease (SCD). Sickle cell anemia (SS), the homozygous state for Hgb S, is the most common and severe form. SCD also includes compound heterozygous states for Hgb S and other hemoglobinopathies, such as Hgb C and β -thalassemia. The gene for Hgb S occurs commonly, but not exclusively, in individuals of African ancestry. In the United States, 9% of African Americans have sickle cell trait and 1 in 600 has SS.^{1,2}

Individuals with SCD have a shortened life expectancy. In 1994, the National Institutes of Health (NIH)-sponsored Cooperative Study of SCD (CSSCD) estimated that the median survival for individuals with SS was 42 years for men and 48 years for women.³ SCD-related mortality in childhood contributed significantly to this shortened survival. Thirty years ago, for example, only one half of children with SCD were expected to reach adulthood.⁴ Improvements in the medical care of children with SCD have since increased their survival.^{5,6} These measures include early diagnosis by newborn screening (NBS), prophylactic penicillin (PCN) to prevent fatal pneumococcal sepsis, parental education, and comprehensive medical care.⁷ More recent advancements include hydroxyurea,⁸ stem cell transplantation,⁹ and expansion of chronic transfusion programs.¹⁰

Accurate survival data for children with SCD facilitate treatment and counseling of patients and their families, guide public health interventions, and provide the foundation for future

Reprints: Charles T. Quinn, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390; e-mail: charles.quinn@utsouthwestern.edu.

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research. The best method to measure overall survival is a cohort study. Because SCD may cause death in young children, optimal cohorts should include only subjects identified at birth or in the first few months of life. Reports from Jamaica and the CSSCD^{11,12} describe the 2 SCD cohorts that meet this criterion, but their seminal findings are now aging. Accrual to these cohorts began 25 to 30 years ago, before widespread use of prophylactic PCN, universal NBS for hemoglobinopathies,^{13,14} the advent of hydroxy-urea and stem cell transplantation, and the increasing use of chronic transfusion therapy. The forward-looking design of the Jamaican cohort included universal NBS.

We sought to determine contemporary survival data for children with SCD that better reflect the impact of modern therapy of SCD. To this end, we defined a newborn inception cohort, the Dallas Newborn Cohort, that included children with SCD who were identified by NBS in the state of Texas and followed in our center up to 18 years of age. All subjects with SS or sickle β^0 -thalassemia ($S\beta^0$) were prescribed prophylactic PCN. We also analyzed clinical stroke as one indicator of SCD-related morbidity.

Patients and methods

Setting

The Dallas Pediatric Sickle Cell Program is located in Children's Medical Center Dallas on the campus of the University of Texas Southwestern Medical Center at Dallas (UT Southwestern). It is the referral center for children with SCD in most of northeast Texas. Its catchment area includes a pediatric population of approximately 1.3 million, including both urban and rural communities. Two rural outreach clinics are also held regularly in Tyler and Paris, Texas.

Since 1977, we have uniformly prescribed oral prophylactic PCN for children with SS and $S\beta^0$, until at least 5 years of age. Since 1995, we have discontinued PCN prophylaxis for children older than 5 years, except for those who had prior pneumococcal sepsis, a surgical splenectomy, or whose caregivers preferred to continue prophylaxis. For individuals who stop PCN prophylaxis, we prescribe a home supply of penicillin (500 mg by mouth 3 times daily for 3 days) to be administered at the onset of low-grade fever (37.8–38.4°C [100–101.4°F]). Regardless of PCN prophylaxis status, all patients and families are instructed to seek immediate medical attention for any temperature of 38.5°C (101.5°F) or greater.

Our center's policy now is to immunize all children with SCD with 2 doses of the 23-valent pneumococcal polysaccharide vaccine at 2 and 5 years of age. Since the heptavalent-conjugated pneumococcal vaccine (Prevnar; PCV-7; Wyeth Pharmaceuticals, Collegeville, PA) was licensed, our policy has been to ensure that all infants with SCD received 4 doses of PVC-7, according to the guidelines of the American Academy of Pediatrics.¹⁵ For older children who did not receive PCV-7 in infancy, we administer 2 doses of PCV-7 at least 2 months apart for those under 5 years of age and 1 dose for those 5 years of age and older. The conjugated *Hemophilus influenzae* type b vaccine has also been administered since 1988 according to American Academy of Pediatrics guidelines for all children.¹⁵

Universal NBS for hemoglobinopathies in Texas began November 1, 1983. We initially evaluate children as soon as possible after diagnosis and schedule children with SS and $S\beta^0$ to be evaluated in our clinics every 3 to 4 months when younger than 3 years of age, every 4 to 6 months from 3 to 5 years of age, and every 6 to 12 months thereafter. Children with sickle-hemoglobin C disease (SC) and sickle β^+ -thalassemia ($S\beta^+$) are scheduled to be evaluated in the clinic every 4 to 6 months when younger than 5 years of age and every 6 to 12 months thereafter. Patients are followed in our center until 18 years of age.

Chronic transfusion therapy is uniformly instituted for the prevention of recurrent stroke, and it is also used in select patients with severe disease characterized by frequent pain or recurrent acute chest syndrome. We first used hydroxyurea in August 1992, and it is prescribed on an individual basis for patients with frequent pain or recurrent acute chest syndrome when chronic transfusions are not preferred by the patient and family. Two individuals in our center have undergone stem cell transplantation, both for the prevention of recurrent stroke after initial chronic transfusion therapy.

Definition of the cohort

We defined the Dallas Newborn Cohort to include all children who were (1) born in Texas on or after November 1, 1983; (2) identified to have a form of SCD by the NBS program of the Texas Department of Health^{16,17}; (3) evaluated at least once in our center; (4) and confirmed to have either SS, SC, S β° , or S β^{+} . Every child who met these criteria was included in this study. SCD genotypes were determined by review of NBS results, serial blood counts, peripheral blood morphology, hemoglobin electrophoresis, and, if necessary, family or molecular genetic studies. We did not include in the cohort less common SCD genotypes, such as sickle-Hgb D-Punjab (Los Angeles) disease, sickle-Hgb O-Arab, and sickle-hereditary persistence of fetal hemoglobin (S-HPFH).

Collection of data

Subjects were tracked prospectively using our center's comprehensive SCD database. A paper-based database was created in 1977, and it was converted to a computer-based version in 1982. The database records the genotype, method and date of diagnosis, demographic data, records of immunization, steady-state hematologic parameters, and dates of all known SCD-related complications, hospitalizations, and transfusions. The current status of each patient is indicated by continually updated status codes: (1) active (evaluated in our center within the past 2 years); (2) inactive (not evaluated in the past 2-5 years); (3) lost to follow-up (not evaluated in the past 5 or more years); (4) moved; (5) deceased; (6) transitioned to adult medical care; or (7) currently receiving a program of chronic transfusion therapy. All subjects were entered into the database on their first evaluation in our center. The Institutional Review Board of UT Southwestern approved the use of the database for this project and decided that informed consent was not required.

Deceased subjects were identified by a status code in the database. Causes of death were determined by review of medical records and, when available, autopsy reports. Subjects who had a stroke were identified by query of the database and medical records. A stroke was defined as an acute neurologic syndrome lasting more than 24 hours that was caused by cerebral vascular occlusion or hemorrhage and documented by radiographic imaging. Transient ischemic attacks (events lasting < 24 hours) and clinically "silent" strokes were not included, regardless of radiographic findings. Accurate dates of all deaths and strokes were known.

Statistical analysis

Because individuals with SS and S β° tend to have a more severe clinical course than those with SC and S β^{+} , we divided the cohort into these 2 groups for separate analysis. We defined 3 measures of outcome: (1) death from any cause; (2) death at least partially attributed to SCD; and (3) clinically overt first stroke. We calculated the overall and age-specific incidence rates for each outcome and used the Kaplan-Meier method to estimate survival from each outcome through 18 years of age.¹⁸ Entry into the cohort was defined as the date of birth. Surviving subjects were censored on the date of their last clinic visit or hospitalization at our center. We did not censor any period of observation for individuals who received hydroxyurea (n = 29), chronic transfusion therapy (n = 31), or stem cell transplants (n = 2) because we aimed to measure the impact on survival of all contemporary therapies, from PCN to transplantation.

Kaplan-Meier survival curves were compared by the log-rank test.¹⁸ Categorical and continuous variables were compared with the Fisher exact test and the 2-tailed Mann-Whitney test, respectively.

Results

Subjects

The Dallas Newborn Cohort includes 711 individuals with SCD observed through August 1, 2002 (Table 1). The median age of subjects on their first evaluation in our center was 4.2 months (range, 0.8–173.8 months). The median age at first evaluation was lower for subjects with SS and S β° (3.9 months; range, 0.9–171 months) than for SC and S β^{+} (5.0 months; range, 0.8–173.8 months; $P = .013$). The median follow-up for the entire cohort was 7.4 years (range, 0.1–18.9 years). The median follow-up was longer for subjects with SS and S β° (7.9 years; range, 0.1–18.9 years) than for SC and S β^{+} (6.9 years; range, 0.1–17.7 years; $P = .026$). Among cohort members who were not known to be deceased, individuals with SC and S β^{+} were more likely to be inactive or lost to follow-up than those with SS and S β° (64 [24.6%] of 260 versus 47 [11%] of 426; $P < .0001$), which accounts for the shorter median follow-up of the SC and S β^{+} subjects. The mean age at loss to follow-up was 3.6 years (range, 0.1–10.8 years) for SS and S β° and 5.0 years (range, 0.8–11.6 years) for SC and S β^{+} subjects.

Events

There were 25 deaths (Table 2). Fifteen deaths were at least partly attributed to SCD, and 10 were apparently unrelated to SCD. The mean age at death was 5.6 years. All SCD-related deaths occurred in SS subjects. Four subjects died of pneumococcal sepsis, all before the conjugated pneumococcal vaccine was available. Three of the 4 isolates of pneumococcus from these subjects were sensitive to both PCN and cephalosporins; sensitivities were not available for the remaining isolate from the subject who died at 2.5 years of age. The 2 children who were younger than 5 years of age had been prescribed prophylactic PCN. One of the 2 children older than 5 years had remained on PCN until his death at age 5.4 years. All families reported compliance with the twice daily regimen of PCN. For the subject who died of pneumococcal sepsis at 6 years of age, the interval between discontinuation of PCN and death was approximately 12 months. The death from *H influenzae* type b sepsis also occurred before the vaccine for *Hemophilus* was available. We previously described the deaths from ceftriaxone-induced hemolysis¹⁹ and myocardial infarction.²⁰ All known deaths are included. No subject is known to have died after being censored for this analysis.

There were 30 clinically overt first strokes; all occurred in SS subjects. Twenty-seven strokes were infarctive and 3 were hemorrhagic. The median age at the time of first infarctive stroke was 4.2 years (range, 0.6–12.7 years). First hemorrhagic stroke occurred in individuals aged 1.4, 12.5, and 12.7 years. One subject had an infarctive stroke at 3.3 years of age, and he later died of complications of recurrent strokes at 7.8 years.

Table 3 shows for SS and S β° subjects the overall and age-specific incidence rates of death, SCD-related death, and stroke. For SC and S β^{+} subjects, the overall incidence of death was 0.24/100 patient-years, and there were no SCD-related deaths or strokes.

Survival analysis

Survival curves for subjects with SS and S β° are shown for each of the 3 outcomes (Figure 1A-C). Table 4 provides an age-specific, tabular summary of the survival data for individuals with SS and S β° . Among the SS and S β° subgroup, there was no difference in survival between boys and girls (overall survival, $P = .85$). The SC and S β^{+} subgroup (survival curves not shown) had a predicted overall survival of 97.4% at 18 years of age (95% confidence interval [CI]:

93.9, 100); SCD-related and stroke-free survival were 100% at 18 years. SC and S β^+ subjects had significantly better survival than those with SS and S β^o (overall survival, $P = .02$).

Discussion

The survival of children with SCD has been studied by different methods, including analyses of death certificates^{21,22} and longitudinal demographic surveys.^{3,23–25} However, the best method to assess overall SCD-related mortality is a cohort study. The ideal cohort includes only subjects who are followed from birth,²⁶ because infants and young children can die from SCD. The Jamaican cohort study of SCD^{12,27} is the only previously published newborn inception cohort. All subjects in this cohort were identified by NBS. The infant cohort of the CSSCD comprised the subjects who were enrolled on the CSSCD before 6 months of age and followed for up to 10 years.¹¹ Entry into the CSSCD cohort was not defined by identification through NBS. In 1986, after the initiation of both cohorts, a randomized clinical trial demonstrated the lifesaving benefit of prophylactic PCN for young children with SCD.¹⁴ Because PCN prophylaxis became routine thereafter, early subjects in the Jamaican and CSSCD cohorts may have died of infections that are prevented today.

The Dallas Newborn Cohort is unique (Table 5). It is the largest newborn inception cohort of children with SCD, and it includes individuals with the 4 common SCD genotypes: SS, SC, S β^+ , and S β^o . All subjects were identified by NBS, and all children with SS and S β^o were prescribed prophylactic PCN. The care of the subjects in the Dallas cohort was coordinated by a single center, like the Jamaican cohort, but unlike the multi-institutional CSSCD. Dallas subjects were from rural and urban communities in the United States, like the CSSCD and Jamaican cohorts. The initial subjects in the Dallas cohort have recently entered adulthood, and accrual to this cohort and the prospective collection of data continue. Although an exact comparison of survival among these 3 cohorts is difficult because of diverse methods of collection and analysis of data, a simple comparison of the survival curves is shown in Figure 1D.^{11,12}

The overall incidence of death among subjects with SS and S β^o in the Dallas cohort was 0.59/100 patient-years compared to 1.1/100 patient-years in the CSSCD infant cohort. This lower death rate might partly be due to the longer period of follow-up and the different age structure of the Dallas population. For example, the report of the CSSCD infant cohort included relatively little follow-up beyond 6 years of age.¹¹ Considering only the first 6 years of life in the Dallas cohort, to better compare with the CSSCD, the death rate was 0.81/100 patient-years. No incidence densities (eg, events/100 patient-years) were reported from the Jamaican cohort. In a longitudinal study of children and adolescents from the CSSCD, Leiken and colleagues reported an overall death rate of 0.62/100 patient-years in SS subjects.²³ However, this population included all subjects who were younger than 20 years of age on entry to the CSSCD, which would underestimate the true childhood death rate. A large, longitudinal survey from Los Angeles, which included observation during the 25 years preceding 1990, reported a death rate of 3/100 patient-years for children with SS in the first 5 years of life.^{24,28} In summary, the death rate in the Dallas Newborn Cohort is lower than past determinations.

The proportion of deaths from infection was 50% in the CSSCD infant cohort, 28% in Jamaica, and 20% in Dallas. Four Dallas subjects died of pneumococcal sepsis. Two of these deaths occurred in children older than 5 years of age, when PCN prophylaxis is typically discontinued,²⁹ including one child who had remained on PCN. All occurred before the heptavalent-conjugated pneumococcal vaccine (PCV-7) was licensed. The recent, widespread use of PCV-7 will likely further reduce the risk of invasive pneumococcal disease in children with SCD, including those older than 5 years who do not take PCN. The death from *H influenzae* type b sepsis also occurred before that vaccine was available. After infection, the most common causes

of death in the Dallas Newborn Cohort were the acute chest syndrome and multiorgan failure syndrome. No subject was known to have died of acute splenic sequestration. The peak age of death has also increased. The most common ages of death were 0.5 to 1 year in Jamaica,^{12, 30} 1 to 3 years in CSSCD,^{11,23} and 4 to 6 years in the Dallas Newborn Cohort.

First clinical stroke in the Dallas cohort occurred most frequently between 2 and 8 years of age, which is consistent with past CSSCD data.^{11,31} The incidence of stroke in the Dallas cohort is also comparable to other studies. Ohene-Frempong and colleagues estimated that the chance of having a clinical stroke by the age of 20 was 11% for individuals with SS in the CSSCD.³¹ Similarly, we estimate that 11.5% of individuals with SS or S β° will have a stroke by 18 years of age. The Jamaican cohort study reported that 7.8% of patients had a stroke by age 14 years.³²

The outcome of subjects with SC and S β^{+} was significantly better than those with SS and S β° . There were no ostensibly SCD-related deaths in this subgroup, and none had a clinically overt stroke. We report an overall death rate of 0.21/100 patient-years for the SC and S β^{+} group. Leiken and colleagues reported a death rate of 0.2 and 0/100 patient-years for individuals with SC and S β^{+} , respectively, who entered the CSSCD before 20 years of age.²³ No patient in the CSSCD infant cohort with SC or S β^{+} died or had a stroke.¹¹

This study has a number of potential limitations. Some infants who were identified by NBS might have died before their initial evaluation in our center. Although the median age of first evaluation in our center is 4 months, an age before which SCD-related death would be unusual, we also collaborate with primary care physicians of most identified newborns to begin PCN prophylaxis before this initial evaluation. To address this issue fully, we would need to extend the analysis of survival to the entire state of Texas, which is presently beyond the scope of our abilities. Loss to follow-up may also bias the survival data, and it is possible that we did not ascertain all events. Our rate of loss to follow-up is relatively small at 4% (inactive 12%). Subjects with SC and S β^{+} were more likely to be lost to follow-up and were younger at the time of loss than subjects of other genotypes, so it is possible that more adverse outcomes may have been missed in this subgroup. However, SC and S β^{+} subjects have a clearly lower risk of death and stroke than those with SS and S β° . We also censored individuals at the time of their last clinic appointment or hospitalization for the survival analysis. Such censored data can underestimate the true survival rate. There also appears to be a greater than expected number of deaths from causes unrelated to SCD in this cohort. This may represent an ascertainment bias of our tertiary care center, an increased risk of fatal complications from any illness or injury in individuals with SCD, or both. Finally, we did not study other morbid outcomes, such as recurrent acute chest syndrome and frequent painful episodes, in part because their definitions are subjective and not standardized. Death and clinically overt stroke are more objective and easily measured.³³

The decreased death rate, decreased number of fatal infections, and the increased mean age at death confirm that NBS and prophylactic PCN have been effective for the very young. However, the advent of effective, conjugated vaccines against the pneumococcus and *H influenzae* type b as well as the increasing use of disease-modifying therapies, such as hydroxyurea, stem cell transplantation, and chronic transfusions, may have also improved the survival of the Dallas Newborn Cohort. The magnitude of each intervention's survival benefit cannot be measured easily, but, in aggregate, contemporary therapy has improved the survival of children with SCD. The survival estimates from our study also reflect the availability of specialized SCD-related care, which does not, unfortunately, apply to very child with SCD in the United States. However, the natural history of untreated SCD is known. We believe that the care of all children with SCD in the United States should be coordinated by a referral center

with expertise in management of SCD and that this care should begin as soon as affected babies are identified by universal NBS programs.

This contemporary snapshot of the survival of children with SCD reveals that mortality has decreased, the mean age at death has increased, and fewer die of infection. These encouraging findings highlight both current successes and the ongoing need to improve the care of older individuals with SCD. For example, acute chest syndrome has become the most common cause of death due to SCD, and better treatment is needed. Moreover, because mortality is decreasing, there is an urgent need for new therapies to decrease the morbidity of SCD. The long-term follow-up of individuals with SCD is now more important, and the Dallas Newborn Cohort will be a powerful tool to monitor survival into early adulthood and to identify predictors of outcome.

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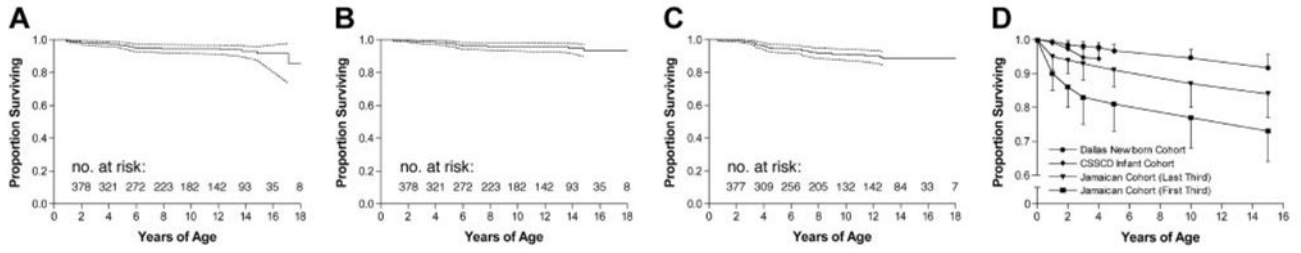


Figure 1. Survival of children with SS and Sβ°

Shown are overall survival (A), SCD-related mortality (B), and stroke-free survival (C). Numbers above the x-axes indicate the number of subjects remaining at risk at a particular age. Dotted lines delimit the 95% CIs. (D) Overall survival curves for the Jamaican cohort study of SCD (SS only), the CSSCD infant cohort (SS only), and the Dallas Newborn Cohort (SS and Sβ°). Vertical bars indicate upper or lower boundaries of the 95% CIs (one direction omitted for clarity). The survival curve for the CSSCD infant cohort was published for approximately 4 years of observation.¹¹ The Jamaican cohort was divided into thirds based on date of birth. Subjects in the first third (1973–1975) did not routinely receive prophylactic PCN, whereas subjects in the middle (1975–1979) and last (1979–1981) thirds did receive PCN. Survival curves are shown only for the first and last third of the Jamaican cohort.

Table 1

Characteristics of the Dallas Newborn Cohort

Genotype	SS	Sβ°	SC	Sβ⁺	Total
No.	431	17	215	48	711
Male, %	53.1	64.7	47.0	54.2	51.6
Patient-years of observation	3571	144	1632	301	5648
Status, no.					
Active	305	8	145	38	496
Inactive	33	3	44	6	86
Lost to follow-up	11	0	12	2	25
Moved	32	5	10	0	47
Deceased	22	0	2	1	25
Transitioned to adult care	4	0	2	1	7
Chronic transfusions currently	24	1	0	0	25

Table 2
Deaths in the cohort

Cause of death	No.	Genotype	Age at death, y
Probably related to SCD			
Pneumococcal sepsis	4	SS	2.5, 3.1, 5.4, 6.0
Acute chest syndrome	3	SS	4.8, 5.5, 5.8
Multiorgan failure syndrome	2	SS	4.8, 14.8
<i>H influenzae</i> type b sepsis	1	SS	1.9
Myocardial infarction	1	SS	13.7
Complications of recurrent strokes	1	SS	7.8
Ceftriaxone-induced hemolysis	1	SS	2.0
Multifactorial	2	SS	0.9, 4.0
Total	15		4.8*
Probably unrelated to SCD			
Motor vehicle collision	2	SS, SC	1.8, 1.9
Drowning	1	SS	1.2
Complex congenital heart disease (CHD)	1	SS	1.0
Acute viral myocarditis	1	SS	1.1
Down syndrome, Hirschsprung disease, complex CHD	1	SS	5.2
Glutaric acidemia type 2	1	SS	12.1
Closed head injury	1	SS	17.1
$\gamma\delta$ -T-cell lymphoma	1	SC	12.1
Metabolic disorder	1	S β^+	1.7*
Total	10		1.9*

* Median age.

Table 3
Incidence of death and stroke among SS and Sβ° subjects

Age group, y	Incidence, no. events/100 patient-years		
	Death	SCD death	Stroke
0-2	0.72	0.24	0.24
2-4	0.43	0.43	1.67
4-6	1.36	1.19	1.08
6-8	0.20	0.20	1.31
8-10	0.00	0.00	0.27
10-12	0.00	0.00	0.68
12-14	0.87	0.44	0.95
14-16	0.81	0.81	0.00
16-18	2.91	0.00	0.00
Overall	0.59	0.40	0.85

Table 4

Tabular summary of survival data for subjects with SS and Sβ°

Age	Overall survival		SCD-related survival		Stroke-free survival	
	% survival	95% CI	% survival	95% CI	% survival	95% CI
6 mo	100	—	100	—	100	—
1 y	99.5	98.8–100	99.8	99.3–100	99.8	99.3–100
2 y	98.5	97.3–99.7	99.5	98.8–100	99.5	98.8–100
4 y	97.7	96.2–99.2	98.6	97.5–99.9	96.3	94.3–98.3
6 y	95	92.7–97.3	96.3	94.2–98.4	94.3	91.8–96.8
8 y	94.6	92.1–97.1	95.9	93.7–98.1	91.3	88.0–94.6
10 y	94.6	92.1–97.1	95.9	93.7–98.1	91.6	88.4–94.5
12 y	94.6	92.1–97.1	95.9	93.7–98.1	90.1	86.5–93.7
14 y	93	89.7–96.3	94.9	92.0–97.8	88.5	84.3–92.7
16 y	91.7	87.6–95.8	93.6	89.8–97.4	88.5	84.3–92.7
18 y	85.6	73.4–97.8	93.6	89.8–97.4	88.5	84.3–92.7

— indicates not applicable.

Table 5

Comparison of neonatal and infant SCD cohorts

Cohort	Dates of enrollment	No. of subjects		Patient-years of observation		Age at entry	Uniform PCN prophylaxis	Ongoing accrual
		Total	SS	Total	SS			
Jamaica	1973–1981	563	315	NR	NR	Birth (NBS)	No	No
CSSCD	1978–1988	694	427	2908	1781	< 6 mo	No	No
Dallas	1983–2002	711	431	5648	3571	Birth (NBS)	Yes	Yes

NR indicates not reported.