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# Sickle Cell Disease in Pregnancy: Maternal Complications in a Medicaid-Enrolled Population

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### Abstract

Higher frequencies of pregnancy complications have been reported among women with sickle cell disease (SCD) compared with those without SCD; however, past studies are limited by small sample size, narrow geographic area, and use of hospital discharge data. We compared the prevalence of maternal complications among intrapartum and postpartum women with SCD to those without SCD in a large, geographically diverse sample. Data from the 2004–2010 Truven Health MarketScan<sup>®</sup> Multi-State Medicaid databases were used to assess the prevalence of maternal complications among intrapartum and postpartum women 15–44 years of age with and without SCD whose race was reported as black. The comparison group of women without SCD was further divided into those with chronic conditions associated with multi-organ failure and those without chronic conditions. Multivariable log-binomial regression models were used to calculate adjusted prevalence ratios for outcomes for women with SCD compared with women in the two comparison groups. Of the 335,348 black women with a delivery during 2004–2010, 1,526 had a diagnosis of SCD (0.5 %). Compared with women without SCD who had chronic conditions, women with SCD had higher prevalence of deep vein thrombosis, pulmonary

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embolism, obstetric shock, pneumonia, sepsis, postpartum infection, and transfusions. SCD was also positively associated with acute renal failure, cerebrovascular disorder, respiratory distress syndrome, eclampsia, postpartum hemorrhage, preterm birth, and ventilation when compared with women without SCD and chronic conditions. Overall, women with SCD have increased prevalence of pregnancy complications, even when compared with a group of women with similar risk for multi-organ failure.

#### **Keywords**

Sickle cell disease; Sickle cell anemia; Pregnancy; Pregnancy complications

### Introduction

Sickle cell disease (SCD) is an inherited hemoglobinopathy that affects approximately 80,000–100,000 Americans in the US, with the majority of cases among African Americans [1–3]. The primary manifestations of SCD are chronic hemolytic anemia and pain crises due to vaso-occlusion [4, 5]. Repeated vaso-occlusive crises can affect multiple organ systems, and individuals with SCD have increased risk of stroke, renal dysfunction, pulmonary hypertension, retinal disease, and avascular necrosis [3, 5, 6]. In women with SCD, the underlying anemia and multi-organ dysfunction can complicate pregnancy, by affecting the cardiovascular, renal, hematologic, and respiratory systems [4, 7]. Improvements in medical care and treatment for individuals with SCD coupled with advancements in neonatal care have contributed to a decline in morbidity and mortality associated with pregnancy among those with SCD; however, the physiological changes in pregnancy still carry important clinical risk for some patients with SCD [8].

While most studies of SCD and pregnancy outcomes are limited by small sample size and restricted geographic area, two large, population based studies have assessed a variety of maternal and infant outcomes associated with SCD. Barfield et al. conducted a retrospective cohort study of women of African descent who resided in Massachusetts with a live birth or fetal death recorded during 1998-2006 [9]. The authors reported that women with SCD had a higher prevalence of preeclampsia, lung disease, and heart disease during the antenatal, delivery or postpartum periods compared with women without hemoglobinopathies. In addition, the odds of fetal death, preterm birth, low birth weight, and cesarean delivery were higher for women with SCD compared with women with no reported hemoglobinopathies after adjusting for maternal age, education, parity, plurality, insurance status at delivery, prenatal care utilization, smoking and infant gender. Using a nationally representative sample of pregnancy-related discharges during 2000-2003, Villers et al. assessed pregnancy-related complications and comorbidities for deliveries with and without a SCD diagnosis. Compared with deliveries without a SCD diagnosis, those with SCD were more likely to have cerebral vein thrombosis, deep vein thrombosis, pneumonia, sepsis, cesarean delivery, preterm labor, and fetal growth restriction [10]. These studies provide important information on perinatal outcomes for women with SCD; however, the former study included women from only one state and the latter study could not assess the influence of multiple hospitalizations by the same woman during the study period on the results of the

study. In addition, neither study included information on complications diagnosed in the outpatient setting.

Given the limited literature on perinatal outcomes for women with SCD, and the potential impact of additional improvements in modern obstetric care and treatment for SCD, there remains a substantial need for additional studies of pregnancy-associated complications and outcomes for women with SCD. The primary aim of this study was to use a longitudinally linked, multi-state health insurance claims database to assess the prevalence of maternal complications during the intrapartum and postpartum periods for a cohort of women with and without SCD.

#### Methods

The data used for this analysis were obtained from the 2004–2010 Truven Health MarketScan<sup>®</sup> Multi-State Medicaid databases, which contain individual level, de-identified healthcare claims information from Medicaid enrollees in multiple states [11]. These data contain information across the continuum of care (e.g. inpatient admissions, outpatient services, and outpatient pharmaceutical claims) as well as data on race, age and gender that are collected as part of the monthly enrollment record. Every enrollee is assigned a unique identifier that facilitates the tracking of individual patients across all types of claims and over multiple years. During 2010, the Multi-State Medicaid database contained information on more than 6.4 million enrollees residing in twelve unidentified states.

All women aged 15–44 years with a delivery hospitalization during 2004–2010 were included. A delivery hospitalization was defined as any inpatient hospital admission record with an International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) code for a pregnancy-related diagnosis or procedure (V27.x, 650, 669.7, 72.0, 72.1, 72.21, 72.29, 72.31, 72.39, 72.4, 72.51–72.54, 72.6. 72.71, 72.79, 72.8, 72.9, 73.22, 73.59, 73.6, 74.0–74.2, 74.4, or 74.99) or a diagnosis-related group (DRG) code for vaginal or cesarean delivery (370–375 for DRG version 24 and earlier or 765–782 for DRG version 25 and later) [12]. Records were excluded if the diagnosis contained codes or procedures for hydatidiform mole, ectopic pregnancy, other abnormal products of conception, or abortion (ICD-9-CM codes 630, 631, 632, 633.x, 634.x–638.x, 639.x, 69.01, 69.51, 74.91, or 75.0). If more than one delivery occurred during the study period, data from the first delivery only was used for the analysis. The postpartum period was defined as the first 8 weeks after the index delivery hospitalization. In order to allow for 8 weeks of follow up for all women, deliveries occurring after October 31, 2010 were excluded from the analysis.

Sickle cell disease was identified by the presence of an ICD-9-CM code for SCD (282.41, 282.42, or 280.60–282.69) recorded in any position during an inpatient (15 diagnostic fields available) or outpatient (2 diagnostic fields available) encounter occurring between 2004 and 2010. All inpatient SCD diagnoses were considered valid. Diagnoses noted on outpatient claims without a corresponding inpatient diagnosis were included only if the diagnosis was listed on more than 1 claim at least 30 days apart. The analysis was further restricted to women whose race was reported as black due to comparatively low prevalence of SCD in US non-black populations [1, 2].

The comparison group of black women without SCD was categorized into two mutually exclusive populations characterized by the presence or absence of selected chronic conditions. The chronic conditions were chosen based on their association with multi-organ failure, with the assumption that such conditions may present similar risks as SCD for the pregnancy outcomes assessed in this study [13]. Thus, by creating a comparison group with similarly increased prevalence of organ damage, we could theoretically more effectively assess the additional risks for maternal complications that may be due to SCD and not attributable to the effects of multi-organ failure. The chronic conditions were identified by ICD-9-CM codes and included type 1 diabetes, essential hypertension, pulmonary hypertension, congenital heart defects, cardiomyopathy, systemic lupus erythematous, viral hepatitis (B and C), epilepsy, and hypothyroidism (see "Appendix"). Because these conditions can affect multiple organ systems, we did not group them according to organ system. The first comparison group (CC+) was composed of women with any of the selected conditions reported during any inpatient or outpatient encounter prior to the delivery admission or during the postpartum period. As before, diagnoses based on outpatient claims alone were included only if present on more than one claim and the interval between claims was 30 days. The other comparison group (CC-) was composed of women without any of the aforementioned chronic conditions reported in their claims data. Women with other types of hemoglobinopathies, including thalassemia (282.49) and unspecified hemoglobinopathies (282.7), were excluded from both comparison groups.

ICD-9-CM codes were also used to identify maternal complications that were categorized as medical, obstetrical and infectious; these complications and selected procedures (see "Appendix") were included if reported during an emergency room visit, the index hospitalization, any postpartum hospitalization, or any outpatient postpartum encounter for women with and without SCD. The complications were not mutually exclusive; thus, women could have more than one complication reported. Maternal age at delivery was derived from the inpatient claim associated with the delivery hospitalization. Plurality (651.x or V27.2–V27.7) and smoking (305.1 or 649.0) were ascertained during any inpatient or outpatient encounter in the 40 weeks prior to the delivery hospitalization. As before, 1 claim noted 30 days apart was required for outpatient diagnoses.

All analyses were conducted using SAS 9.2 (Cary, NC). Two-tailed Chi square tests or ttests were used to compare the distribution of maternal characteristics and complications among black women with SCD and the two comparison groups of black women without SCD. Multivariable log-binomial regression models were used to calculate prevalence ratios for maternal complications for women with SCD compared with the CC+ and CC– comparison groups, after adjusting for maternal age at delivery, plurality and smoking 40 weeks prior to the delivery hospitalization.

#### Results

From 2004 to 2010, there were 335,348 Medicaid-enrolled women whose race was reported as black and who had a delivery admission; of those, 1,526 (0.5 %) had a diagnosis of SCD. Among black women without SCD (n = 333,822), 6.6 % had one or more chronic conditions associated with multi-organ failure. Overall, women with SCD tended to be younger than

those without SCD, but the difference was more pronounced among those with chronic conditions (Table 1). Approximately 3 % of women with SCD had a multiple birth compared with about 2 % of women in either comparison group. The prevalence of tobacco use was similar between women with SCD and those in the CC+ group (5 %) but was lower for women in the CC– group (3.5 %). The mean length of stay during the delivery hospitalization of 4.7 days for women with SCD was significantly longer compared with 4.1 and 2.9 days for women in the CC+ and CC– groups, respectively.

Table 2 depicts the prevalence of maternal complications during the intrapartum and postpartum period for women with SCD and those without SCD. Compared with the CC+ group, women with SCD had significantly higher frequencies of deep vein thrombosis, pulmonary embolism, obstetric shock, eclampsia, and major perineal laceration. With the exception of pyelonephritis, the prevalence of all infectious conditions was higher among women with SCD than among women in the CC+ group. Approximately 13 % of women with SCD had a transfusion during the intrapartum or postpartum period, compared with 2 % of CC+ women. Women in the CC+ comparison group had a higher prevalence of cesarean delivery (48.3 %) than women with SCD (43.3 %) and a lower prevalence of operative vaginal delivery (18.5 % vs. 24.0 %). Compared with the CC– group, women with SCD had significantly higher prevalence for all outcomes assessed except placental abruption, uterine atony, premature rupture of membranes, major perineal laceration and obstetric trauma.

With the exception of cesarean delivery, all associations noted in the bivariate analysis remained statistically significant after adjusting for maternal age, plurality, and tobacco use. For example, women with SCD were at least twice as likely to be diagnosed with deep vein thrombosis or pulmonary embolism during the intrapartum or postpartum period compared with women in the CC+ group (Table 3). No differences between women with SCD and women in the CC+ group were found in the prevalence of acute renal failure, cerebrovascular disorder, or respiratory distress. Compared with the CC+ group, women with SCD had significantly higher prevalence of obstetric shock (aPR 2.67, 95 % CI 1.71–4.18) and all infectious complications except pyelonephritis. Women with SCD also had lower prevalence of eclampsia (aPR 0.51, 95 % CI 0.45–0.59) and higher prevalence of transfusion (aPR 5.21, 95 % CI 4.43–6.12) and operative vaginal delivery (aPR 1.45 95 % CI 1.34–1.56) than women in the CC+ group.

Compared with women in the CC– group, women with SCD were approximately 8 times more likely to have a diagnosis of cerebrovascular disorder, deep vein thrombosis, and respiratory distress syndrome, and 10 times more likely to have pulmonary embolism (Table 3). Having SCD was positively associated with a number of obstetric complications such as obstetric shock (aPR 10.18, 95 % CI 6.78–15.30), eclampsia (aPR 2.25, 95 % CI 1.98–2.57), postpartum hemorrhage (aPR 1.47, 95 % CI 1.17–1.85), wound complications (aPR 2.25 95 % CI 1.76–2.89), and preterm birth (aPR 1.34, 95 % CI 1.23–1.45) when compared with the CC– group. Women with SCD were 17 times more likely to have pneumonia and 5 times more likely to have sepsis than women in the CC– group. The prevalence of ventilation procedures (aPR 3.36 95 % CI 2.11–5.33), transfusion procedures (aPR 12.37 95 % CI 10.84–14.11), cesarean delivery (aPR 1.21, 1.18–1.23), and operative vaginal delivery (aPR

1.23, 95 % CI 1.12–1.35) were also higher among women with SCD than their counterparts without chronic conditions. Regardless of comparison group, SCD was not significantly associated with placental abruption, uterine atony, premature rupture of membranes, and obstetric trauma.

### Discussion

Using data from a large, multi-state sample of Medicaidenrolled women, we found that black women with SCD are more likely to have medical, obstetric, and infectious complications during the intrapartum and postpartum period than black women without SCD. Furthermore, the prevalence of several adverse maternal outcomes remained elevated even when compared with a group of women without SCD but with similar risk for multiorgan failure. Although other studies have assessed pregnancy complications associated with SCD, the present study is novel in at least two respects: first, pregnancy outcomes for US women with SCD were compared to those experienced by a group of women likely to be comparably affected by multi-organ failure; and second, the study included complications diagnosed in both the inpatient and outpatient setting.

Overall, our findings confirm those of previous studies [9, 10, 14] and provide further insight into the maternal risks associated with SCD in pregnancy. For example, we found that renal failure, lung disease, eclampsia, and preterm birth were more common among women with SCD, but only when compared with black women without SCD and without chronic conditions. This finding suggests that multi-organ failure associated with SCD may explain the elevated risks for these conditions in women with SCD when compared with the general population of women without SCD, as documented in previous studies [9, 10]. In addition, our finding that black women with SCD have significantly higher prevalence of deep vein thrombosis (DVT) and pulmonary embolism (PE), regardless of the comparison group, suggests that the association between thromboembolic events and SCD may be independent of the processes related to organ damage. Recently, blood transfusion has been recognized as a potential risk factor for venous thromboembolism [15] and may explain these results, given the high rate of blood transfusions among women with SCD.

Thrombosis has also been identified as an important complication of SCD in pregnancy [10, 16] and may be attributable to the hypercoagulable state of those with SCD [17]. Consistent with other studies of SCD [18] and sickle cell trait [19], we found that the risk ratio for pulmonary embolism among women with SCD was higher than the risk ratio for DVT, when compared with women without SCD and without chronic conditions. However, when compared with the chronic conditions group, women with SCD were approximately twice as likely to have either DVT or PE. The preponderance of PE in relation to DVT among women with SCD compared with the general population of women without SCD may reflect the underlying physiological changes associated with SCD which can be manifested by widespread microvascular obstruction leading to interruption of normal perfusion and function of organs such as the lungs [8]. However, when compared with women with similar risk for organ damage, we found that the risk for DVT and PE was comparable, suggesting that the effects of hypercoagulability are not substantially different for the lungs in comparison with other regions of the body.

Similar to previous studies, we also found an increase in the prevalence of nearly all infectious complications among women with SCD when compared to their counterparts without SCD. This phenomenon is likely due to the reduced humoral immune response secondary to functional or surgical asplenism which predisposes people with SCD to encapsulated bacterial infections [20]. Interestingly, we did not find a significant difference in the prevalence of pyelonephritis among women with SCD when compared with women in the CC+ group. This finding may be explained by the renal dysfunction seen in women with SCD and in many of the chronic conditions in the comparison group which may result in a

The present study was subject to several limitations. First, it is likely that some misclassification according to SCD status was present, despite using data from multiple years to ascertain SCD diagnoses. Furthermore, we were unable to assess differences in maternal complications according to SCD genotype because this information cannot be reliably detected using ICD-9-CM codes. Variations in the risk of adverse pregnancy outcomes according to SCD genotype have been reported with lower frequencies of maternal and fetal complications among women with HbSC disease than women with homozygous HbSS [7, 14]. The implication of this limitation is that the prevalence of complications for certain subgroups may be overestimated or underestimated.

similarly increased prevalence of pyelonephritis.

Next, because ICD-9-CM codes were also used to ascertain chronic conditions and maternal outcomes, these indicators may have also been affected by inaccurate coding. While the validity of code-based obstetric diagnoses in discharge databases is variable, findings from a recent study indicated that specificity for nearly all pregnancy related comorbidities was 98 % or greater and false negative errors occurred with a higher frequency than false positives [21]. Therefore, the associations reported herein may understate or overstate the true association.

Also, because the distribution of age for women without SCD who had chronic conditions was skewed toward older ages compared with women with SCD, it is possible that the effect measures were modified by age when comparing the prevalence of maternal complications for these two groups of women. When age was included as an interaction term in the adjusted models, no statistically significant evidence of interaction was observed; however, small sample size precluded the meaningful interpretation of some models.

Finally, because the data include only those women enrolled in Medicaid, our findings may not be representative of privately insured or uninsured women with SCD. Although studies have shown that inpatient hospital, outpatient hospital, or emergency department visits did not differ significantly between a national sample of privately insured and Medicaidenrolled adults after controlling for health status and other factors [22], higher rates of health services utilization have been reported for Medicaid-enrolled children with SCD compared their privately insured counterparts [23]. We were also unable to identify the states from which the Medicaid sample was drawn and, therefore, could not assess the effects of regional variations in the management and treatment of SCD or pregnancy.

While advances in obstetric care and the treatment of SCD have contributed to significant declines in maternal and perinatal mortality rates, women with SCD continue to have increased risk for pregnancy complications compared with those without SCD. Moreover, having SCD may confer additional risks for adverse maternal outcomes beyond those typically associated with multi-organ failure. Therefore, efforts must be made by both clinical and public health providers to improve pregnancy outcome for women with SCD. Targeted preconception health interventions such as enhanced screening for chronic disease complications, reviewing and updating immunization status, genetic counseling, smoking cessation, and optimizing hemoglobin and hematocrit levels prior to pregnancy would provide opportunities to improve pregnancy outcomes for women with SCD.

In addition, the National Heart, Lung, and Blood Institute (NHLBI)'s Division of Blood Diseases and Resources and the Centers for Disease Control and Prevention's Division of Blood Disorders formed an interagency agreement to improve the ability to identify and register— with permission—every person in the United States who has a hemoglobinopathy, in an effort to determine where best to focus research and education efforts. The NHLBI is also developing guidelines for medical professionals treating people who have SCD. These guidelines, in combination with the national registry, will provide better information on how to advance the quality of life for those with SCD and thus improve their pregnancy outcomes [24].

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#### Appendix

See Table 4.

# Table 1

Characteristics of intrapartum and postpartum women with and without sickle cell disease

	SCD (N =	1,526)	$= 1,526) \qquad N_0 \text{ SCD, CC+}^a (N = 21,982)$	$CC^+a$ (N		No SCD, CC- $^{b}$ (N = 311,840)	с- <i>р</i> (N	= 311,840)
	Z	%	N	%	$p$ value $^{\dagger}$	N	%	$p$ value $^{\dagger}$
Age at delivery								
15-24	955	62.6	7,206	32.8	<0.001	188,676	60.5	0.04
25–34	507	33.2	10,887	49.5		105,821	33.9	
35-44	64	4.2	3,889	17.7		17,343	5.6	
Plurality								
Singleton	1,474	96.6	21,426 97.5	97.5	0.04	304,678	98.2	<0.001
Multiple birth	52	3.4	556	2.5		5,669	1.8	
Tobacco use $^{c}$	75	4.9	1,102	5.0	0.86	10,938	3.5	0.003
Delivery length of stay (mean days, SD)	4.7 (6.1)	. <u>1</u> .	4.1 (5.2)	2)	0.001	2.9 (3.0)	e	<0.0001

 $a^{u}$ ,CC+" denotes women without SCD who had report of a chronic condition any time prior to delivery

 $^b,\mathrm{CC}\mathrm{--}\mathrm{''}$  denotes women without report of SCD or a chronic condition

 $^{c}$ Report of tobacco use 40 weeks prior to delivery admission

Table 2

Prevalence of maternal complications among women with and those without sickle cell disease

N         %         N         % $p$ value*         N           al complications         10         0.7         216         0.9         0.21         313           ar disorder         12         0.8         185         0.8         0.82         312           ar disorder         17         1.1         118         0.5         0.0001         799           ar disorder         23         2.0         117         0.5         0.0001         799           or disorder         25         1.4         0.5         0.0001         799         930           or disorder         24         1.6         1.1         0.8         <0.0001         18,189           or disorder         28         1.4         0.50         0.004         343           k         24         1.6         1.1         0.5         0.001         18,189           monthage         69         4.5         2.5         0.001         18,189         0.5           k         21.1         1.1         1.18         0.5         0.001         18,189           feations         26         1.8         2.5         1.4         0.1         2.4400	N         %         N           10         0.7         216           12         0.8         185           17         1.1         118           17         1.1         118           17         1.1         118           17         1.1         118           17         1.1         118           17         1.1         118           17         1.1         118           17         1.1         118           17         1.1         118           18         1.1         1.1           198         13.0         5,571           69         4.5         828           56         3.7         5,181           56         3.7         5,181           56         3.7         5,181           69         4.5         562           119         7.8         1,072           19         1.3         86           19         1.3         86		<pre>&gt; value<sup>*</sup> 0.21 0.82 &lt;0.0001 0.004 0.50 &lt;0.0001</pre>	N 313 312 799 799 343 630 630 18,189	0.1	<i>p</i> value <sup>†</sup>
10         0.7         216         0.9         0.21         313           12         0.8         185         0.8         0.82         312           30         2.0         181         0.8         6.0001         799           30         2.0         181         0.8         6.0001         799           31         1.1         118         0.5         0.004         343           24         1.1         118         0.5         0.0001         470           198         13.0         5.571         25.3         <0.0001         470           27         1.8         5.571         25.3         <0.0001         18.189           69         4.5         828         3.8         0.14         9.516           1         1.8         5.571         25.3         6.0001         8.762           360         3.9         9.30         4.2         0.57         5.516           60         3.9         9.14         0.11         38.400         1           61         2.3         5.181         2.3.6         0.94         5.519           51         2.3         5.114         0.11         38.400 </th <th>10     0.7     216       12     0.8     185       30     2.0     181       17     1.1     118       17     1.1     118       25     1.4     313       24     1.6     117       198     13.0     5.571       69     4.5     828       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     5.515       60     3.9     930       60     3.9     930       60     3.9     930       61     2.3.7     5.181       62     3.7     5.181       63     4.5     5.65       inetritis     34     2.2       19     1.3     86       19     1.3     86</th> <th></th> <th>0.21 0.82 &lt;0.0001 0.004 0.50 &lt;0.0001</th> <th>313 312 799 343 630 630 18,189</th> <th>0.1</th> <th></th>	10     0.7     216       12     0.8     185       30     2.0     181       17     1.1     118       17     1.1     118       25     1.4     313       24     1.6     117       198     13.0     5.571       69     4.5     828       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     930       60     3.9     5.515       60     3.9     930       60     3.9     930       60     3.9     930       61     2.3.7     5.181       62     3.7     5.181       63     4.5     5.65       inetritis     34     2.2       19     1.3     86       19     1.3     86		0.21 0.82 <0.0001 0.004 0.50 <0.0001	313 312 799 343 630 630 18,189	0.1	
10         0.7         216         0.9         0.21         313           at         12         0.8         185         0.8         0.82         312           30         2.0         181         0.8         0.82         312         799           17         1.1         1.18         0.5         0.004         343         343           s syndrome         25         1.4         313         1.4         0.50         630         799           24         1.6         1.17         0.5         <0.0001	10 $0.7$ $216$ $21$ $20$ $181$ $30$ $2.0$ $181$ $17$ $1.1$ $118$ $17$ $1.1$ $118$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $117$ $24$ $1.6$ $1.7$ $27$ $1.8$ $5.571$ $1$ $27$ $1.8$ $27$ $1.8$ $2.515$ $1$ $23.7$ $5.181$ $1$ $23.7$ $5.181$ $1$ $23.7$ $5.181$ $1$ $23.7$ $5.181$ $1$ $23.7$ $5.181$ $11$ $23.7$ $5.181$ $11$ $23.7$ $5.181$ $11$ $23.7$ $5.181$ $11$ $23.7$ $5.181$ $119$ $7.8$ $1.92$ $266$ $3.7$ $5.62$ $119$ $7.8$ $1.305$ $12$ $1.3$ $3.61$ $211$ $1.3$ $3.61$ $122$ $2.66$ $1.13$ $119$ $1.3$ $3.61$ $129$ $1.9$ $1.3$ $129$ $1.9$ $1.3$ $129$ $1.9$ $1.3$ $129$ $1.9$ $1.3$ $129$ $1.9$ $1.3$ <td></td> <td>0.21 0.82 &lt;0.0001 0.004 0.50 &lt;0.0001</td> <td>313 312 799 343 630 470 18,189</td> <td>0.1</td> <td></td>		0.21 0.82 <0.0001 0.004 0.50 <0.0001	313 312 799 343 630 470 18,189	0.1	
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30         2.0         181         0.8         <0.0001         799           17         1.1         118         0.5         0.004         343           17         1.1         118         0.5         0.004         343           17         1.1         118         0.5         0.004         343           28         1.1         118         0.5         0.004         343           24         1.6         117         0.5         <0001	30 $2.0$ 181171.1118171.111818171.1118241.611719813.05,57119813.05,571271.85,571271.85,57128271.836123.75,181embranes744.91,072an281.82,515an281.82,11an281.82,515an281.82,515an281.82,515an281.82,11an281.82,11an281.82,11an281.82,11an7.81,305antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266antitis/metritis342,22266 <td></td> <td>&lt;0.0001 0.004 0.50 &lt;0.0001</td>		<0.0001 0.004 0.50 <0.0001	799 343 630 470 18,189	0.1	<0.0001
17         1.1         118         0.5         0.004         343           ss syndrome         25         1.4         313         1.4         0.50         630           24         1.6         117         0.5         <00001	17       1.1       118         ss syndrome       25       1.4       313         24       1.6       117         24       1.6       117         24       1.6       117         24       1.6       117         23       198       13.0       5,571         26       69       4.5       828         27       1.8       525         60       3.9       930         11abor forces       195       12.8       2,515         11abor forces       195       12.8       2,515         and       26       3.7       5,181         an       28       1.8       2,11         an       28       1.8       2,11         an       28       1.8       2,11         an       26       3.7       657         an       28       1.8       2,11         an       28       1.8       2,11         an       26       3.7       657         an       26       3.7       5,52         netritis/metritis       34       2.2       266         netritis/metritis		0.004 0.50 <0.0001	343 630 470 18,189	0.3	<0.0001
ss syndrome         25         1.4         313         1.4         0.50         630 $24$ 1.6         117         0.5         <0.0001	ss syndrome 25 1.4 313 24 1.6 117 24 1.6 117 198 13.0 5,571 27 1.8 525 60 3.9 930 60 3.9 930 60 3.9 930 60 3.9 1.8 525 361 23.7 5,181 embranes 74 4.9 1,072 an 28 1.8 211 an 28 1.8 211 69 4.5 56 netritis/metritis 34 2.2 266 netritis/metritis 34 2.2 266		0.50 <0.0001 <0.0001	630 470 18,189	0.1	<0.0001
	24 1.6 117 198 13.0 5,571 198 13.0 5,571 27 1.8 525 60 3.9 930 27 1.8 525 60 3.9 930 361 23.7 5,181 embranes 74 4.9 1,072 an 28 1.8 211 an 28 1.8 211 69 4.5 56 119 7.8 1,305 119 7.8 1,305 119 7.8 1,305		<0.0001	470 18,189	0.2	<0.0001
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	24       1.6       117         198       13.0       5.571         198       13.0       5.571         27       1.8       5.57         27       1.8       525         60       3.9       930         11abor forces       195       12.8       5.515         11abor forces       195       12.8       2.515         and       361       23.7       5.181         an       28       1.8       2.11         an       28       1.8       2.11         an       28       1.8       2.11         an       28       1.8       2.11         an       26       3.7       657         an       28       1.8       2.11         an       28       1.8       2.11         an       26       3.7       657         netritis/metritis       34       2.2       266         netritis/metritis       34       2.2       266         119       7.8       1.305       1.305		<0.0001	470 18,189		
	198     13.0     5,571       27     18     5,571       27     1.8     525       60     3.9     930       60     3.9     930       11abor forces     195     12.8     2,515       11abor forces     195     12.8     2,515       and     261     23.7     5,181       embranes     74     4.9     1,072       n     28     1.8     2,11       56     3.7     657     657       n     28     1.8     2,11       56     3.7     657       n     28     1.8     2,11       56     3.7     5,52       netritis/metritis     34     2.2     266       119     7.8     1,305       19     1.3     86		<0.0001	18,189	0.2	<0.0001
69 $4.5$ $828$ $3.8$ $0.14$ $9,516$ $27$ $1.8$ $5.25$ $2.4$ $0.12$ $4,762$ $60$ $3.9$ $930$ $4.2$ $0.57$ $5,351$ $11abor forces19512.82,51511.40.1138,400136123.75,18123.60.9451,9201ambranes744.91,0724.90.0615,410n281.82.111.00.0015,631n281.82.111.00.0015,631n281.82.111.00.0015,631n281.82.111.00.0015,631n281.82.111.00.0015,631n281.82.111.00.0016,226n1.91.3860.4<0.00016,226n1.91.3860.4<0.00016,226n1.91.3860.4<0.00012.1693n1.138.31.4396.60.0022.1693n1.1318.31.4396.60.0022.963n1.0534.80.00020.9022.992$	•     69     4.5     828       27     1.8     525       60     3.9     930       11abor forces     195     12.8     2,515       11abor forces     195     12.8     2,515       anbranes     74     4.9     1,072       an     28     1.8     211       an     34     2.2     562       netritis/metritis     34     2.2     266       119     7.8     1.305       12     1.3     86	3.8			5.8	<0.0001
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	27       1.8       525         60       3.9       930         1labor forces       195       12.8       2,515         anbranes       74       4.9       1,072         an       28       1.8       2,11         an       28       1.8       211         an       28       3.7       657         antitis/metritis       34       2.2       266         netritis/metritis       34       2.2       266         119       7.8       1.305       1.305		0.14	9,516	3.0	00000
	60       3.9       930         11abor forces       195       12.8       2.515         361       23.7       5,181         embranes       74       4.9       1,072         n       28       1.8       211         n       28       1.8       211         n       28       1.8       211         n       28       1.8       211         n       26       3.7       657         n       34       2.2       266         netritis/metritis       34       2.2       266         119       7.8       1.305       1.305	2.4	0.12	4,762	1.5	0.44
Ilabor forces19512.8 $2,515$ 11.40.11 $38,400$ 1 $361$ $23.7$ $5,181$ $23.6$ $0.94$ $51,920$ 1 $ambranes$ 74 $4.9$ $1,072$ $4.9$ $0.96$ $51,920$ 1 $m$ $28$ $1.8$ $211$ $1.0$ $0.001$ $5,631$ $5.631$ $m$ $56$ $3.7$ $657$ $3.0$ $0.13$ $14,487$ $7.631$ $69$ $4.5$ $562$ $2.6$ $0.0001$ $6,226$ $metrius/metrius$ $34$ $2.2$ $266$ $1.2$ $0.0006$ $3,125$ $metrius/metrius$ $34$ $2.2$ $266$ $1.2$ $0.0001$ $6,226$ $119$ $7.8$ $1,305$ $5.9$ $0.0006$ $3,125$ $119$ $7.8$ $1,305$ $5.9$ $0.0001$ $221$ $119$ $7.8$ $1,305$ $5.9$ $0.0001$ $221$ $121$ $10.6$ $0.4$ $<0.0001$ $842$ $131$ $8.3$ $1,439$ $6.6$ $0.002$ $12,693$ $121$ $10.53$ $4.8$ $0.0002$ $8,922$	11abor forces     195     12.8     2,515       361     23.7     5,181       embranes     74     4.9     1,072       an     28     1.8     211       an     28     1.8     211       an     28     1.8     211       an     26     3.7     657       69     4.5     562       netritis/metritis     34     2.2     266       119     7.8     1,305       19     1.3     86	4.2	0.57	5,351	1.7	<0.0001
361         23.7         5,181         23.6 $0.94$ 51,920         1           m         28         1.8         1.072 $4.9$ $0.96$ 15,410 $5.631$ m         28         1.8         211         1.0 $0.001$ $5.631$ $5.631$ m         28         1.8         211         1.0 $0.001$ $5.631$ 56 $3.7$ $657$ $3.0$ $0.13$ $14,487$ 69 $4.5$ $562$ $2.6$ $0.0001$ $6.226$ netritis/metritis $34$ $2.2$ $266$ $1.2$ $0.0006$ $3,125$ netritis/metritis $34$ $2.2$ $266$ $1.2$ $0.0006$ $3,125$ $119$ $7.8$ $1.305$ $5.9$ $0.0001$ $221$ $221$ $121$ $0.4$ $0.0001$ $231$ $221$ $221$ $131$ $8.3$ $1.305$ $5.9$ $0.0001$ $221$ $131$ $8.3$ $1.439$	361     23.7     5,181       embranes     74     4.9     1,072       n     28     1.8     211       n     28     1.8     211       56     3.7     657       69     4.5     562       netritis/metritis     34     2.2     266       119     7.8     1,305       19     1.3     86	11.4	0.11	38,400	12.3	0.58
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	embranes 74 4.9 1. an 28 1.8 56 3.7 69 4.5 netritis/metritis 34 2.2 119 7.8 1.	23.6	0.94	51,920	16.6	<0.0001
n         28         1.8         211         1.0         0.001         5,631           56 $3.7$ $657$ $3.0$ $0.13$ $14,487$ 69 $4.5$ $562$ $2.6$ $6.0001$ $6,226$ netritis/metritis $34$ $2.2$ $266$ $1.2$ $0.0006$ $3,125$ netritis/metritis $34$ $2.2$ $266$ $1.2$ $0.0006$ $3,125$ $119$ $7.8$ $1,305$ $5.9$ $0.0003$ $18,330$ $129$ $1.305$ $5.9$ $0.0001$ $221$ $221$ $131$ $8.3$ $1,439$ $6.6$ $0.002$ $12,693$ $131$ $8.3$ $1,439$ $6.6$ $0.002$ $8,992$ $120$ $1.053$ $4.8$ $0.0002$ $8,992$ $8,992$	n 28 1.8 56 3.7 69 4.5 69 4.5 netritis 34 2.2 119 7.8 1.	4.9	0.96	15,410	4.9	0.87
56         3.7         657         3.0         0.13         14,487           netritis/metritis         69         4.5         562         2.6         <0.0001	56 3.7 69 4.5 69 4.5 119 7.8 1, 119 1.3	1.0	0.001	5,631	1.8	0.93
69     4.5     562     2.6     <0.0001     6,226       netritis/metritis     34     2.2     266     1.2     0.0006     3,125       119     7.8     1.305     5.9     0.003     18,330       19     1.3     86     0.4     <0.0001	69 4.5 netritis/metritis 34 2.2 119 7.8 1, 19 1.3	3.0	0.13	14,487	4.7	0.07
tum infection694.5 $562$ $2.6$ $<0.0001$ $6,226$ etritis/endomyometritis/metritis $34$ $2.2$ $266$ $1.2$ $0.006$ $3,125$ annionitis $119$ $7.8$ $1,305$ $5.9$ $0.003$ $18,330$ annionitis $119$ $7.8$ $1,305$ $5.9$ $0.001$ $221$ onia $19$ $1.3$ $86$ $0.4$ $<0.0001$ $221$ $22$ $1.4$ $127$ $0.6$ $<0.0001$ $842$ $ract infection$ $131$ $8.3$ $1,439$ $6.6$ $0.002$ $12.693$ $rinary tract infection$ $106$ $7.0$ $1,053$ $4.8$ $0.0002$ $8,992$	tum infection 69 4.5 etritis/endomyometritis/metritis 34 2.2 amnionitis 119 7.8 1, onia 19 1.3					
etritis/endomyometritis/metritis     34     2.2     266     1.2     0.0006     3,125       ammionitis     119     7.8     1,305     5.9     0.003     18,330       onia     19     1.3     86     0.4     <0.001	etritis/endomyometritis/metritis 34 2.2 amnionitis 119 7.8 1, onia 19 1.3		<0.0001	6,226	2.0	<0.0001
amnionitis 119 7.8 1,305 5.9 0.003 18,330 onia 19 1.3 86 0.4 <0.001 221 22 1.4 127 0.6 <0.001 842 / tract infection 131 8.3 1,439 6.6 0.002 12,693 ininary tract infection 106 7.0 1,053 4.8 0.0002 8,992	annionitis 119 7.8 1,3 onia 19 1.3	1.2	0.0006	3,125	1.0	<0.0001
onia         19         1.3         86         0.4         <0.0001         221           22         1.4         127         0.6         <0.0001	onia 19 1.3	5.9	0.003	18,330	5.9	0.002
22     1.4     127     0.6     <0.0001			<0.0001	221	0.1	<0.0001
131         8.3         1,439         6.6         0.002         12,693           ection         106         7.0         1,053         4.8         0.0002         8,992	22 1.4	0.6	<0.0001	842	0.3	<0.0001
tract infection 106 7.0 1,053 4.8 0.0002 8,992	131 8.3 1	6.6	0.002	12,693	4.1	<0.0001
	106 7.0 1	4.8	0.0002	8,992	2.9	<0.0001
0.6 0.38 1,114	12	0.6	0.38	1,114	0.4	0.005

ompucauon	SCD (N=	<u>= 1,526)</u>	No SCD,	CC+a (L	SCD (N = 1,526) No SCD, CC+ <sup><i>a</i></sup> (N = 21,982)	<u>No SCD, CC-<sup>b</sup> (N = 311,840)</u>	CC- <i>p</i> (N	= 311,840)
	Z	%	Z	%	N % $p$ value <sup><math>\dot{\tau}</math></sup>	Z	%	$\% p$ value $\dot{r}$
Ventilation	18	1.2	356	1.6	356 1.6 0.18	1,042	0.3	1,042 0.3 <0.0001
Transfusion	197	12.9	197 12.9 558 2.5	2.5	5 <0.0001	3,006 1.0	1.0	<0.0001
Cesarean delivery	661	43.3	10,613	48.3	43.3 10,613 48.3 0.0002	91,745	29.4	91,745 29.4 <0.0001
Operative vaginal delivery	366	24.0	4,073	18.5	24.0 4,073 18.5 <0.0001	86,993	27.9	86,993 27.9 0.0007

SCD sickle cell disease, CC chronic conditions (diabetes, pulmonary hypertension, essential hypertension, congenital heart defects, cardiomyopathy, lupus, viral hepatitis, epilepsy and hypothyroidism)

 $\dot{f}$  p value for Chi square test of distribution of variable in SCD group versus distribution in non-SCD group

"CC+" denotes women without SCD who had report of a chronic condition any time prior to delivery

#### Table 3

Adjusted prevalence ratios for the association between sickle cell disease and maternal complications

-	No SCD	$CC_{\perp}a$		
a		,	No SCL	0, CC_ <i>b</i>
a	PR <sup>c</sup>	95 % CI	aPR <sup>c</sup>	95 % CI
Maternal medical complications				
Acute renal failure	0.64	0.34-1.21	6.42	3.42-12.03
Cerebrovascular disorder (	0.85	0.47-1.52	7.92	4.45-14.06
Deep vein thrombosis	2.47	1.67-3.62	7.75	5.40-11.12
Pulmonary embolism	1.96	1.17-3.28	10.27	6.33–16.67
Adult respiratory distress syndrome	1.15	0.77-1.74	7.95	5.28-11.67
Obstetric complications				
Obstetric shock 2	2.67	1.71-4.18	10.18	6.78–15.30
Eclampsia	0.51	0.45-0.59	2.25	1.98-2.57
Postpartum hemorrhage	1.21	0.95-1.55	1.47	1.17-1.85
Placental abruption (	0.74	0.50-1.09	1.14	0.79–1.66
Wound complications (	0.99	0.76-1.28	2.25	1.76-2.89
Uterine atony, abnormal labor forces	0.99	0.86-1.14	1.04	0.92-1.19
Preterm labor/birth	0.99	0.90-1.09	1.34	1.23-1.45
Premature rupture of membranes	1.02	0.81-1.29	0.96	0.77-1.20
Major perineal laceration	1.50	1.01-2.22	1.01	0.70-1.47
Obstetric trauma	1.04	0.79–1.36	0.79	0.61-1.02
Infectious complications				
Postpartum infection	1.47	1.15-1.89	2.22	1.76-2.80
Endometritis/endomyometritis/metritis	1.46	1.02-2.09	2.17	1.56-3.04
Chorioamnionitis	1.21	1.01-1.46	1.31	1.10-1.56
Pneumonia	3.13	1.88-5.21	17.22	10.80-27.44
Sepsis 2	2.42	1.52-3.85	5.25	3.45-8.00
Urinary tract infection	1.23	1.03-1.47	2.09	1.77-2.46
Genitourinary tract infection	1.33	1.09-1.62	2.36	1.96-2.84
Pyelonephritis	1.14	0.63-2.07	2.16	1.23-3.81
Intrapartum/postpartum procedures				
Ventilation	0.64	0.40-1.03	3.36	2.11-5.33
Transfusion	5.21	4.43-6.12	12.37	10.84-14.11
Cesarean delivery (	0.94	0.88-1.00	1.21	1.18-1.23
Operative vaginal delivery	1.45	1.34–1.56	1.23	1.12-1.35

*SCD* sickle cell disease, *CC* chronic conditions (diabetes, pulmonary hypertension, essential hypertension, congenital heart defects, cardiomyopathy, lupus, viral hepatitis, epilepsy and hypothyroidism)

a "CC+" denotes women without SCD who had report of a chronic condition any time prior to delivery

 $^{b}\mbox{``CC-''}$  denotes women without report of SCD or a chronic condition

<sup>C</sup>Adjusted for maternal age, plurality, and tobacco use 40 weeks prior to delivery admission

#### Table 4

ICD-9-CM codes for chronic conditions and maternal and obstetric complications and procedures

	ICD-9-CM codes
Chronic conditions	
Type 1 diabetes mellitus	250.0-250.9
Essential hypertension	401.0-401.9
Pulmonary hypertension	416.0-416.9
Congenital heart defects	745.0–745.9
Cardiomyopathy (hypertrophic obstructive or other primary)	425.1, 425.4
Systemic lupus erythematosus	710.0
Viral hepatitis (B and C)	070.2–070.3, 070.41, 070.44, 070.51, 070.54, 070.70–070.71
Epilepsy	345.0-345.9
Hypothyroidism	244.0-244.9
Maternal medical complications	
Acute renal failure	584, 586, 669.3x
Cerebrovascular disorder	430, 431, 432, 434, 436, 437.6, 674.0x, 671.5x
Deep vein thrombosis	671.3x-671.5x, 671.9x, 451.1, 451.2, 451.81, 453.1, 453.2, 453.40-453.42, 453.8, 453.9
Pulmonary embolism	673.2x, 673.8x, 415.1
Adult respiratory distress syndrome	518.5, 518.81, 518.82, 518.84, 799.1
Obstetric complications	
Obstetric shock	669.1x, 998.0, 995.4, 785.5x
Preeclampsia/eclampsia	642.4x, 642.5x, 642.6x, 642.7x
Postpartum hemorrhage	666.0x-666.3x, 639.1x
Placental abruption	641.2x
Wound complications	674.1x-674.3x
Uterine atony, abnormal labor forces	661.0x-661.9x
Preterm labor/birth	644.0x-644.1x, 644.2x
Premature rupture of membranes	658.1x
Major perineal laceration	664.2x, 664.3x, 664.5x
Obstetric trauma	662.5x-662.9x
Infectious complications	
Postpartum infection	670.xx, 672.xx
Endometritis/endomyometritis/metritis	615.0–615.9
Chorioamnionitis	658.4
Pneumonia	480-483, 485-486, 487.0

	ICD-9-CM codes	
Sepsis	038.x, 995.91, 995.92, 659.3x	
Urinary tract infection	599.0	
Genitourinary tract infection	646.6x	
Pyelonephritis	590.0, 590.1, 590.80	
Intrapartum/postpartum procedures		
Ventilation	93.90, 96.01–96.05, 96.70,	
	96.71, 96.72	
Transfusion	99.00–99.09, V58.2	
Cesarean delivery	74.0, 74.1, 74.2, 74.4, 74.99, 669.7	
Operative vaginal delivery	72.0, 72.1, 72.21, 72.29, 72.39, 72.4, 72.6, 72.71, 72.79, 669.5x	

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