



The Impact of Sickle Cell Status on Adverse Delivery Outcomes Using Electronic Health Record Data

S17: Applied Clinical Research Informatics

Silvia P. Canelón, PhD
University of Pennsylvania
 @spcanelon #IS21

About me



Postdoctoral Research Scientist
University of Pennsylvania

DEPARTMENT OF
BIOSTATISTICS
EPIDEMIOLOGY &
INFORMATICS



*I have no relevant relationships
with commercial interests to disclose*

Principal Investigator

Mary Regina Boland, MPhil, PhD, FAMIA

Collaborator

Samantha Butts, MSCE, MD

Boland Lab

Lena Davidson • Jessica Meeker
Aditya Kashyap • Bernadette D'Alonzo
Becca Morse • Sarah Tadlock • Ella Poole
Jessica Liu • Abigail Bretzin

Learning objectives

Understand how electronic health record (**EHR**) data were leveraged to study the impact of **sickle cell disease** on adverse:

- delivery outcomes including **stillbirth**
- hematological outcomes like **blood transfusion** and **hemorrhage** during delivery.

Motivation

- Pregnant people are often underrepresented in clinical research, as are ethnic and racial minorities
- Those pregnant with sickle cell have been shown to be at an increased risk of adverse outcomes [1]
- The granularity of our dataset enables the study of pregnancy-specific contributions to the risk of a clinical complication at the time of delivery
- We estimate a higher incidence of sickle cell trait at Penn Medicine (~9.8%) compared to national estimates (~7.7%) [2]

1. Barfield WD, Barradas DT, Manning SE, et al. Am J Prev Med. 2010;38:S542–9

2. Centers for Disease Control and Prevention. Data & Statistics on Sickle Cell Disease. 2017

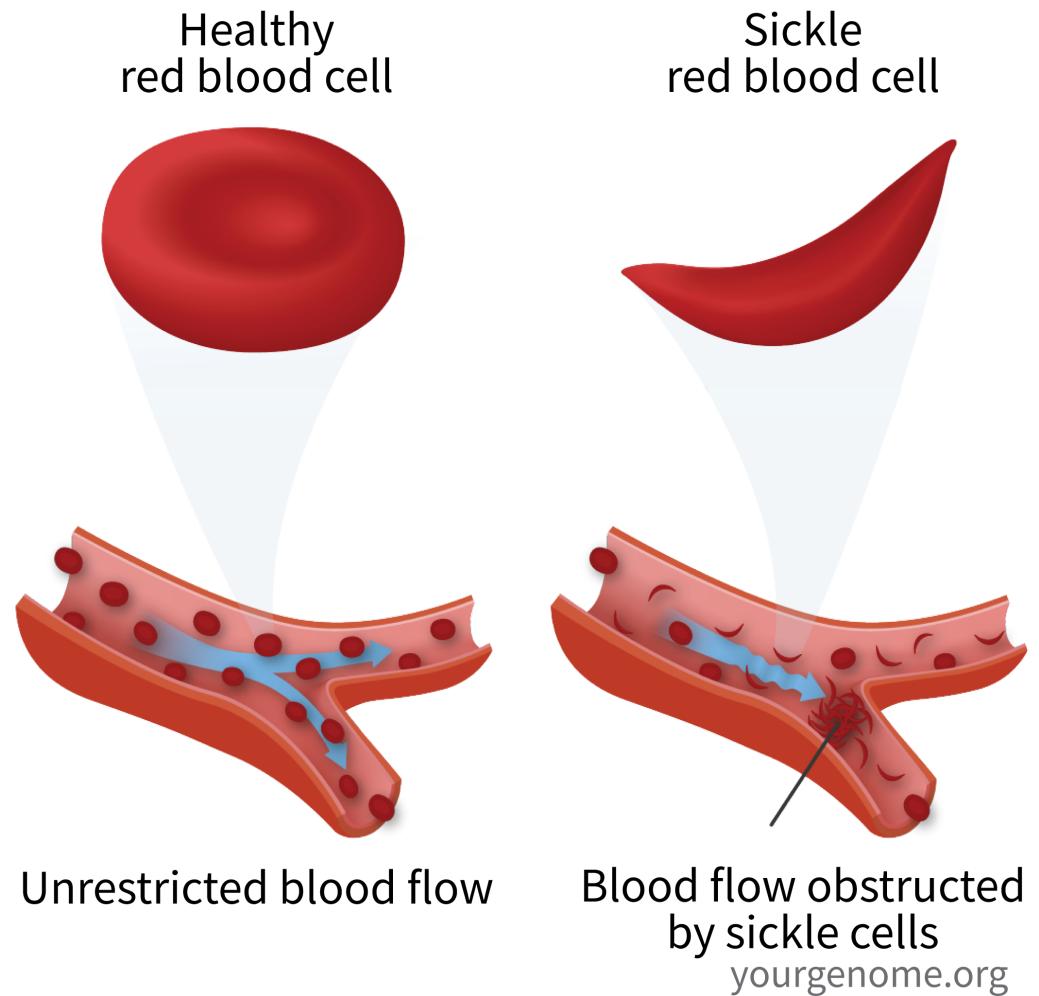
Analysis

1. Used our MADDIE algorithm [1] to identify 63,334 distinct deliveries from EHR of 1,060,000 female patients with visits to Penn Medicine between 2010-2017
2. Identified delivery and hematological outcomes of interest occurring within the patients' delivery episode(s)
3. Constructed **generalized logistic regression model** to assess the risk of a variety of predictors on delivery and hematological outcomes

1. [Canelón et al. Int J Med Inform \(2020\)](#)

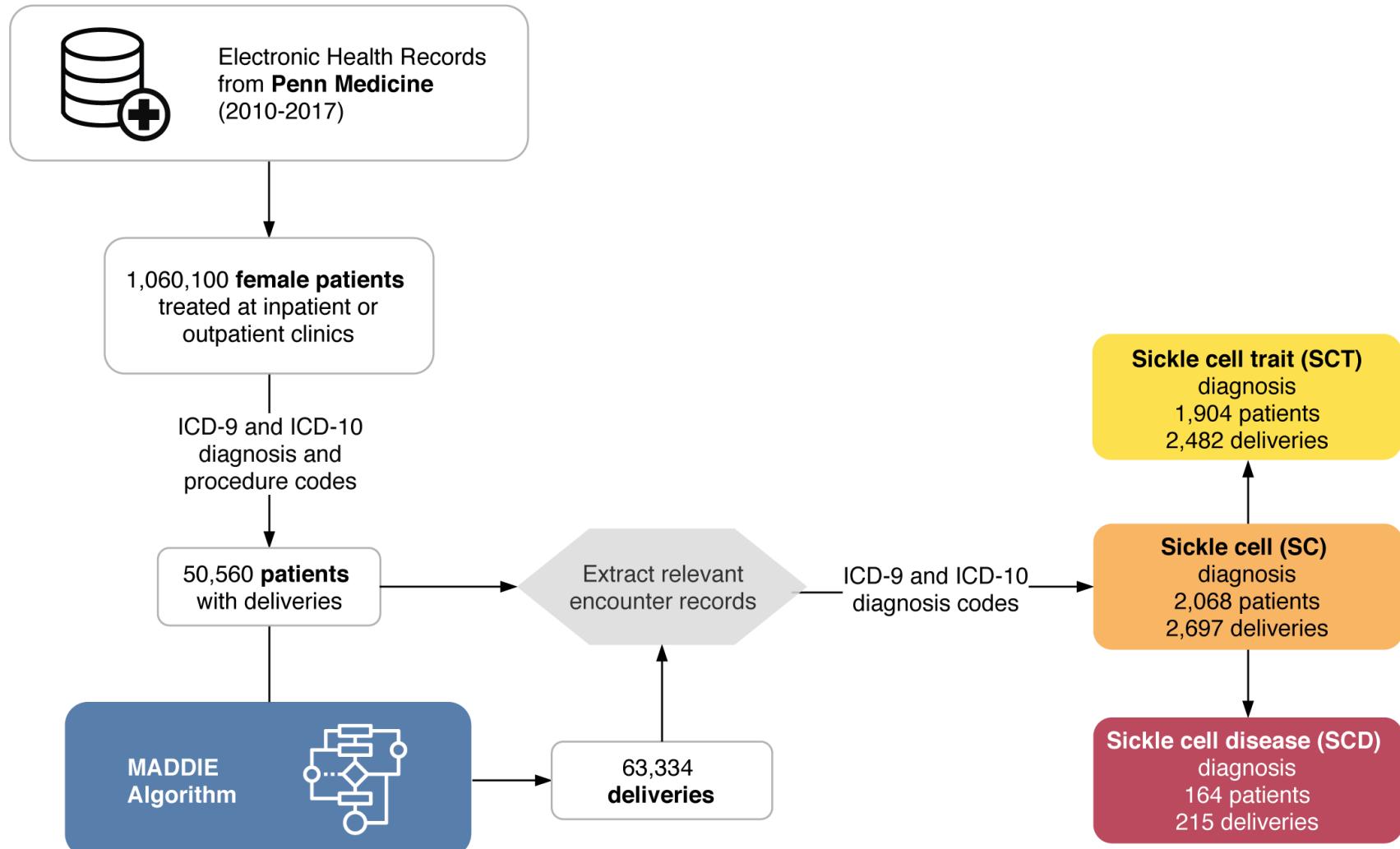
Sickle cell disease

- Complex inherited genetic disorder and most common hemoglobinopathy in the U.S., affecting ~100,000 people [1]
- Primarily affects individuals of African ancestry and is associated with high lifetime morbidity and premature mortality [2]
- Inheriting one hemoglobin S gene results in **sickle cell trait**; inheriting two abnormal genes results in **sickle cell disease**
- The disease is characterized by abnormal hemoglobin and "sickle" red blood cells

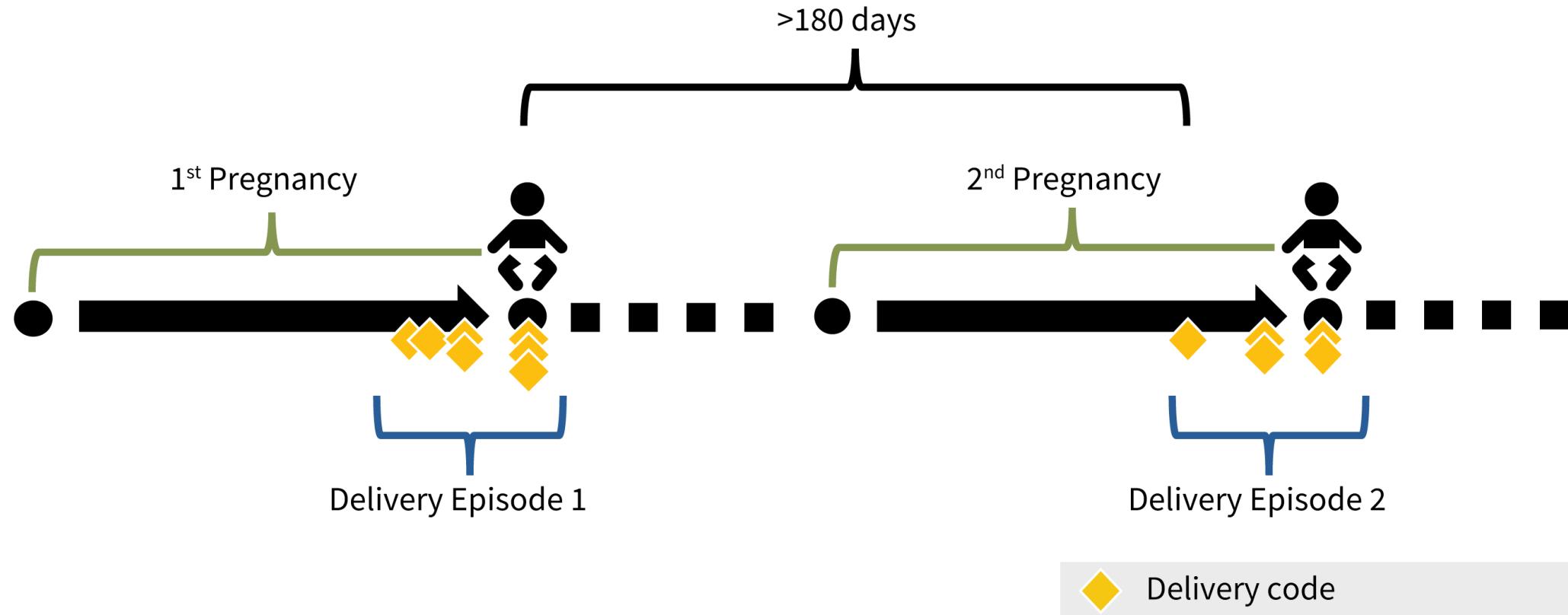


1. Centers for Disease Control and Prevention. Data & Statistics on Sickle Cell Disease. 2017
2. Kuo K, Caughey AB. Am J Obstet Gynecol. 2016;215(4)

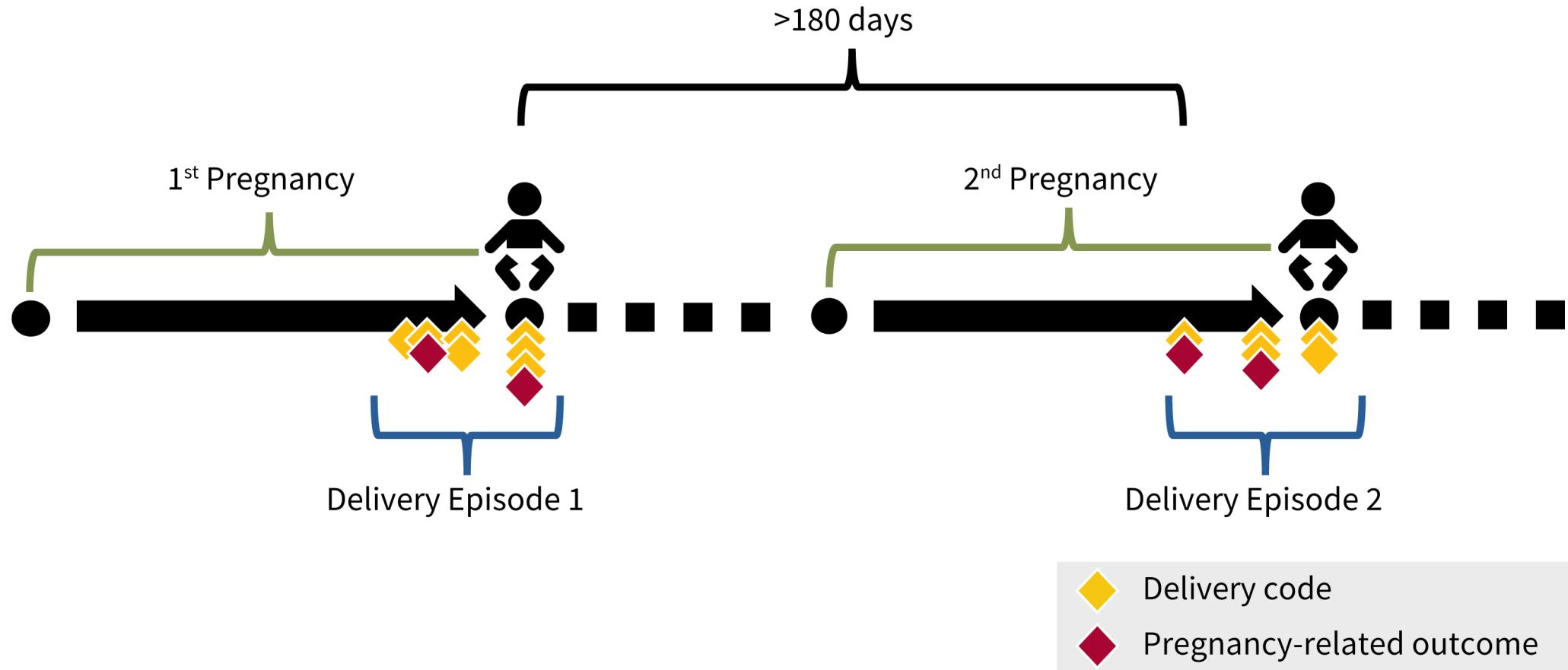
Study overview



Identifying delivery episodes with the MADDIE algorithm



Identifying outcomes within delivery episodes



Patient population at Penn Medicine

	Patients (%)	Deliveries (%)
All Patients	50560 (100.0)	63334 (100.0)
No Sickle Cell	48492 (95.9)	60637 (95.7)
Sickle Cell Mutation	2068 (4.1)	2697 (4.3)
Sickle Cell Trait	1904 (3.8)	2482 (3.9)
Sickle Cell Disease	164 (0.3)	215 (0.3)

Race/Ethnicity	Patients (%)	Deliveries (%)
Sickle Cell Mutation		
All Patients	2068 (100.0)	2697 (100.0)
Hispanic	53 (2.6)	62 (2.3)
Black/African American	1921 (92.9)	2518 (93.4)
Asian	11 (0.5)	14 (0.5)
Other or Mixed	31 (1.5)	40 (1.5)
Unknown	21 (1.0)	22 (0.8)
White	38 (1.8)	49 (1.8)

All race/ethnicity descriptions are 'Non-Hispanic' unless otherwise indicated

Logistic regression model

Delivery outcomes

- C-Section
- Preterm birth
- Stillbirth

Hematological outcomes

- Blood transfusion
- Hemorrhage
- Pain crisis

Predictors

- Sickle cell status (SCT, SCD)
- No. of pain crisis before delivery
- No. of blood transfusions before delivery
- Delivery episode
- Prior C-section
- Multiple birth diagnosis
- Patient age
- Marital status
- Race/ethnicity
- Blood type and blood Rh factor
- Year

Logistic regression model

Delivery outcomes

- C-Section
- Preterm birth
- **Stillbirth**

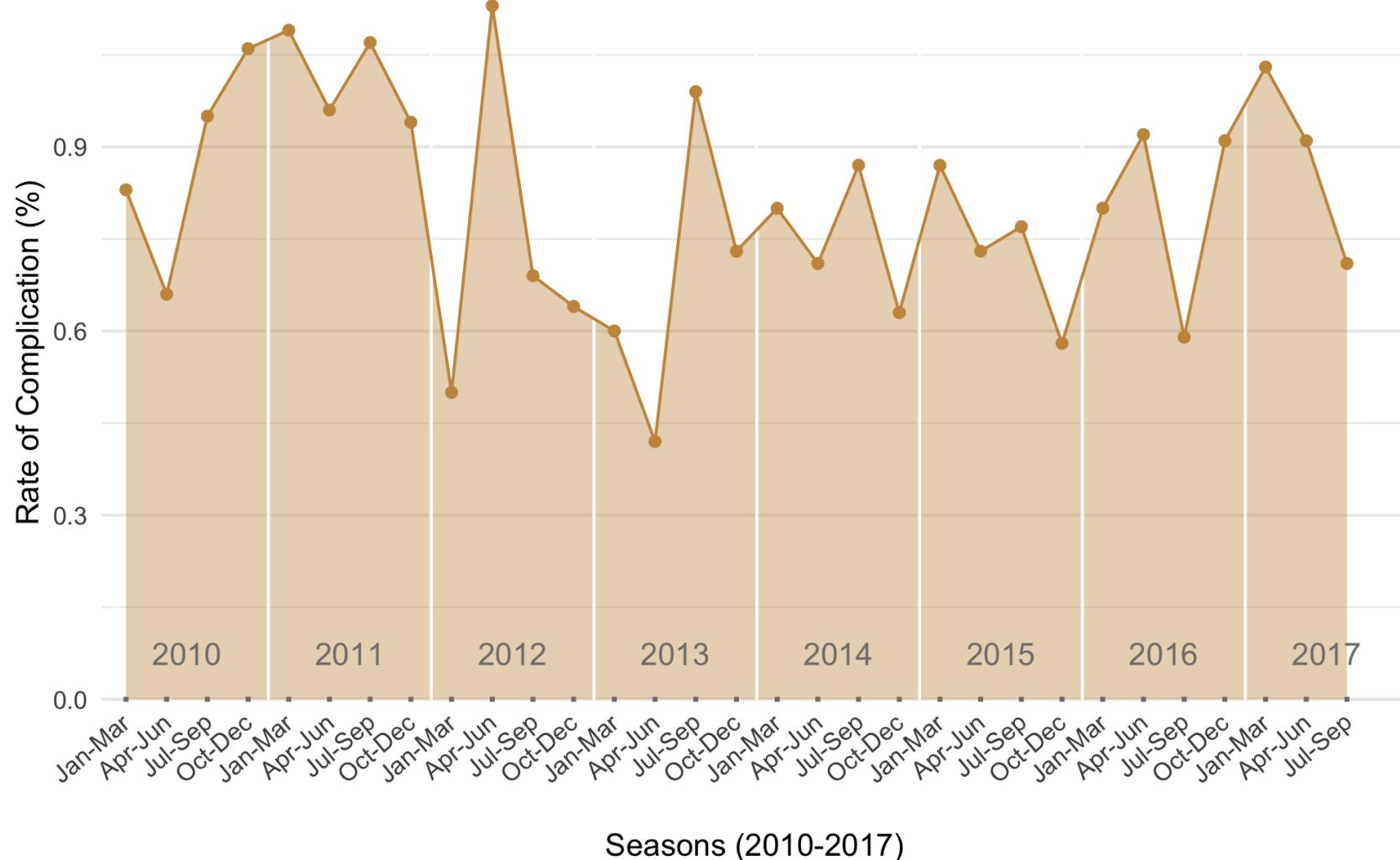
Hematological outcomes

- **Blood transfusion**
- **Hemorrhage**
- Pain crisis

Predictors

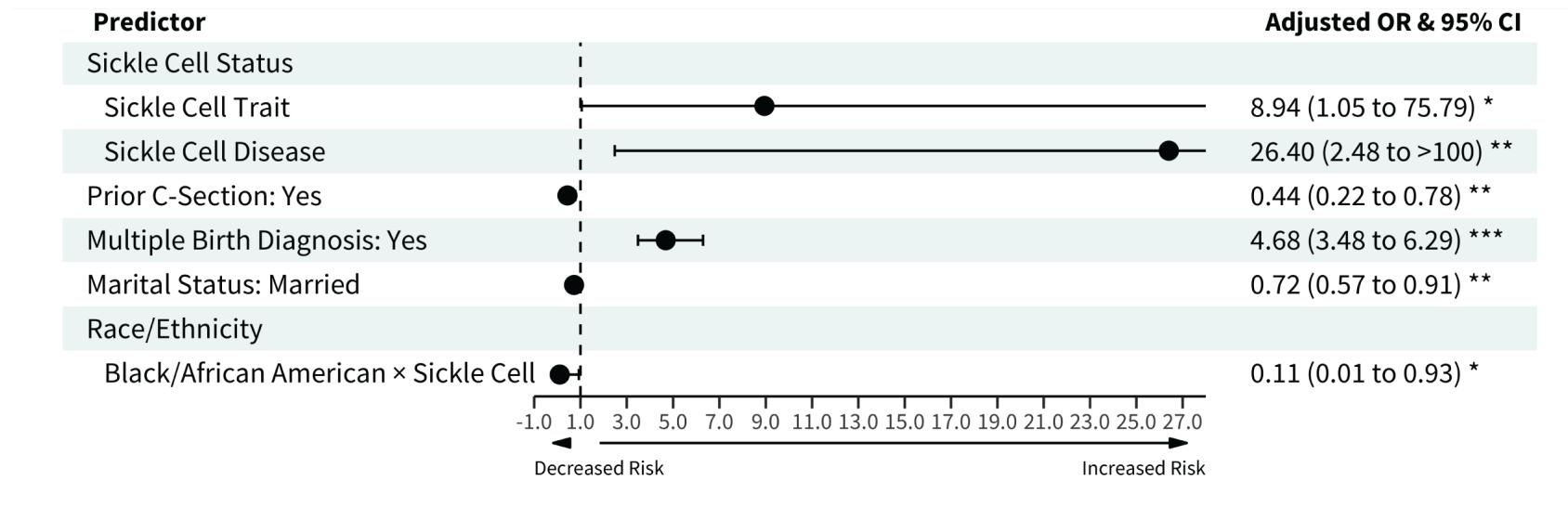
- Sickle cell status (SCT, SCD)
- No. of pain crisis before delivery
- No. of blood transfusions before delivery
- Delivery episode
- Prior C-section
- Multiple birth diagnosis
- Patient age
- Marital status
- Race/ethnicity
- Blood type and blood Rh factor
- Year

Stillbirth: Rates over time



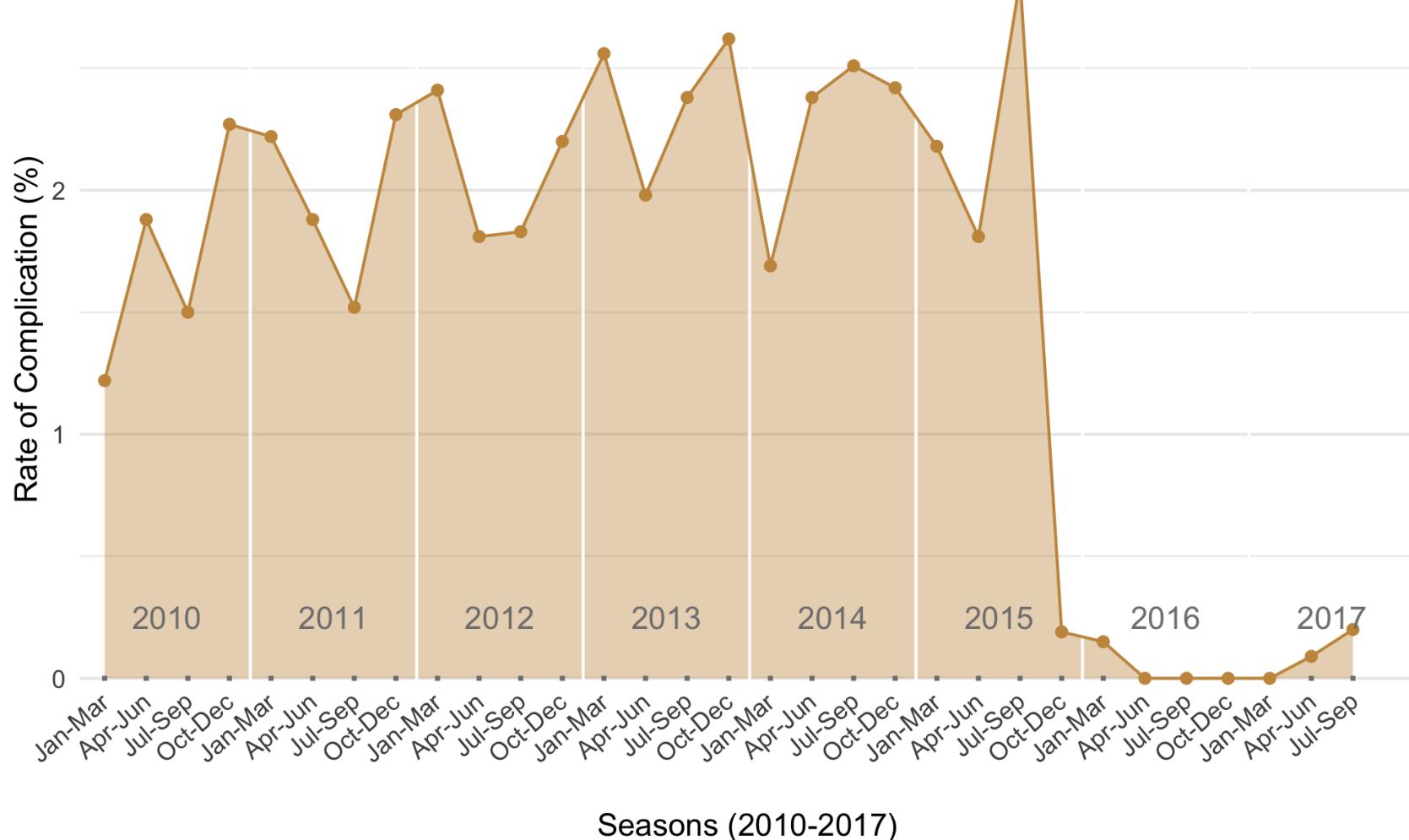
Stillbirth: Model results

Stillbirth: Adjusted odds ratio estimates with 95% confidence intervals



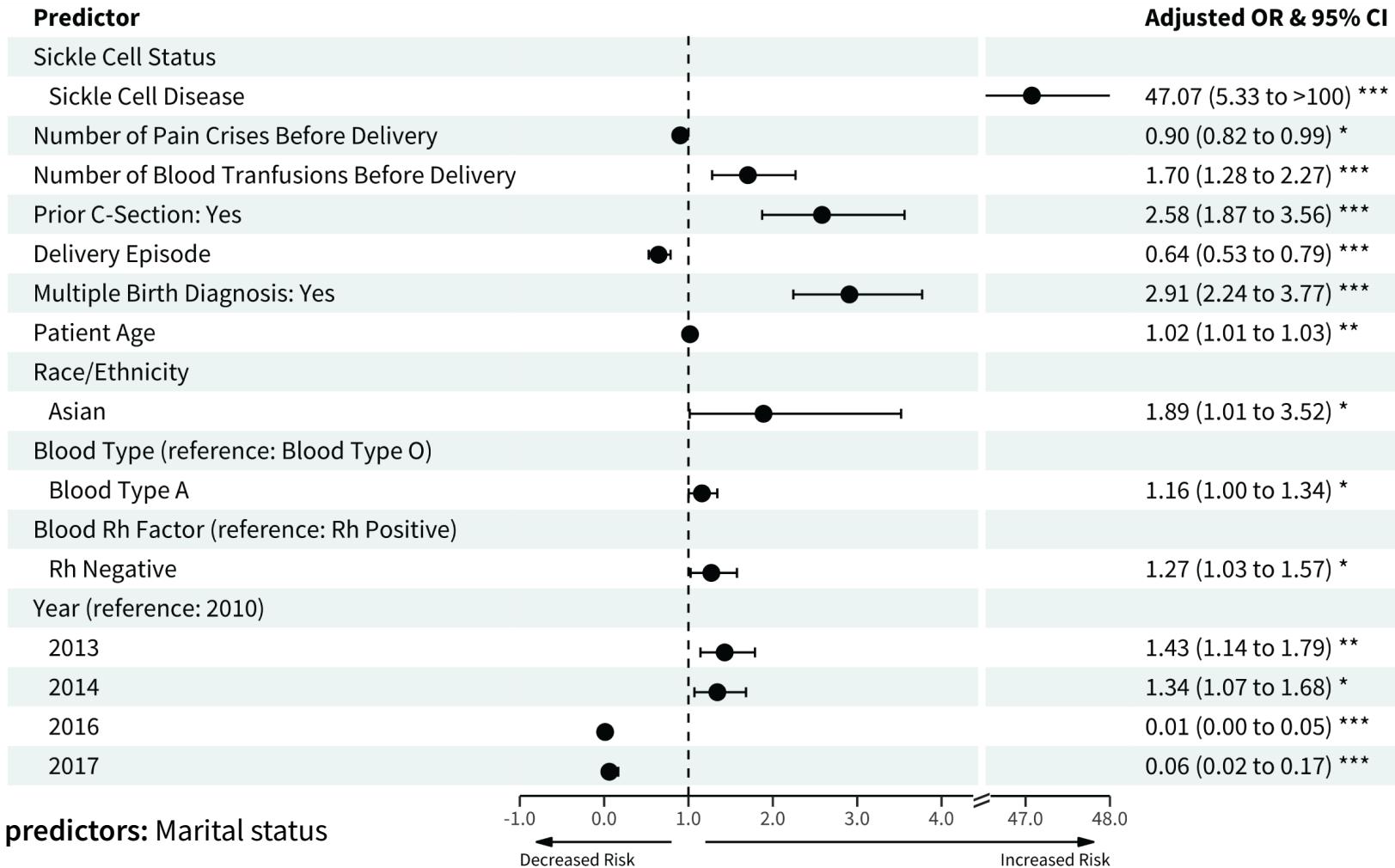
Non-significant predictors: Number of pain crisis before delivery; number of blood transfusions before delivery; delivery episode; patient age; blood type; blood Rh factor, year

Blood transfusion: Rates over time

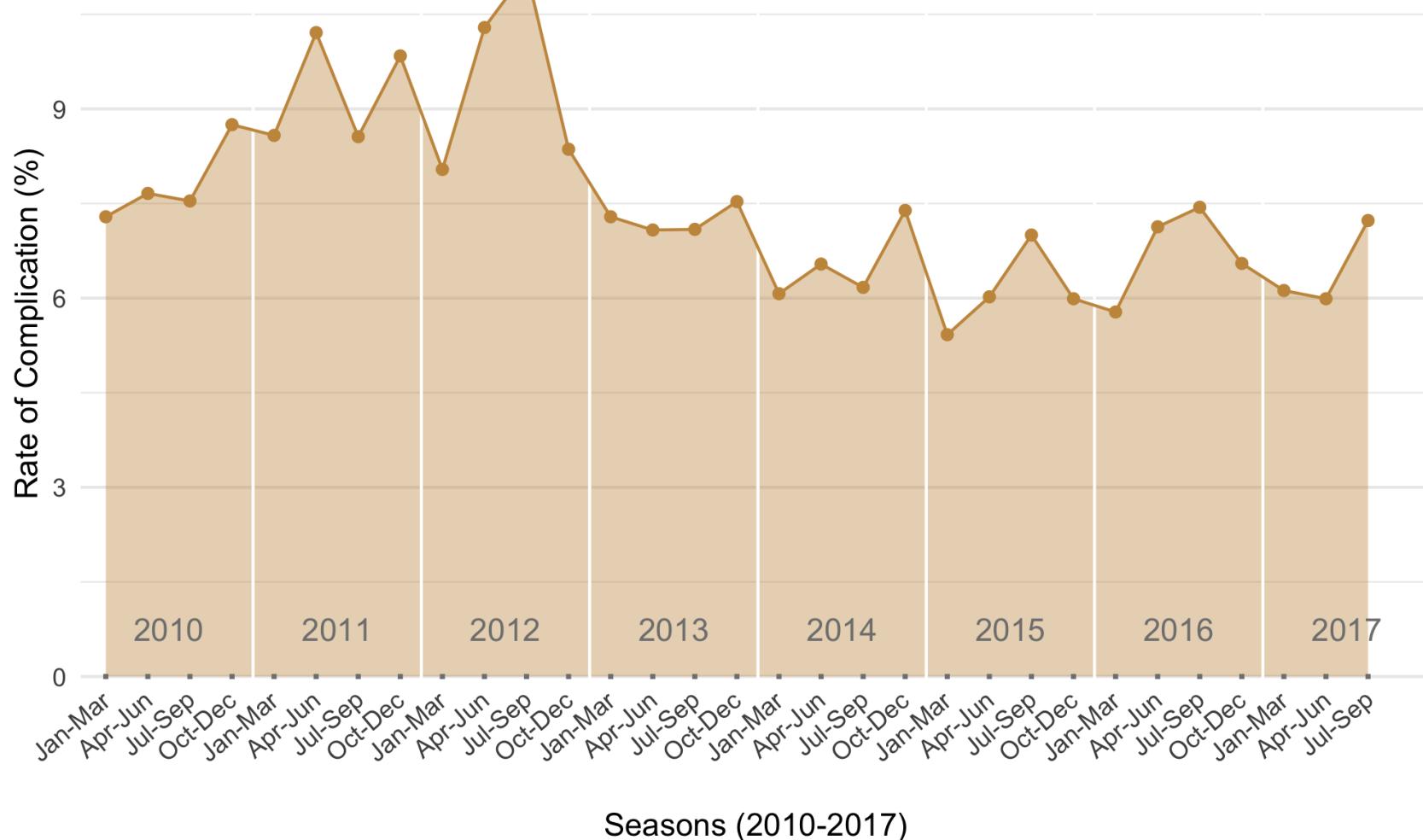


Blood transfusion: Model results

Blood Transfusion During Delivery: Adjusted odds ratio estimates with 95% confidence intervals

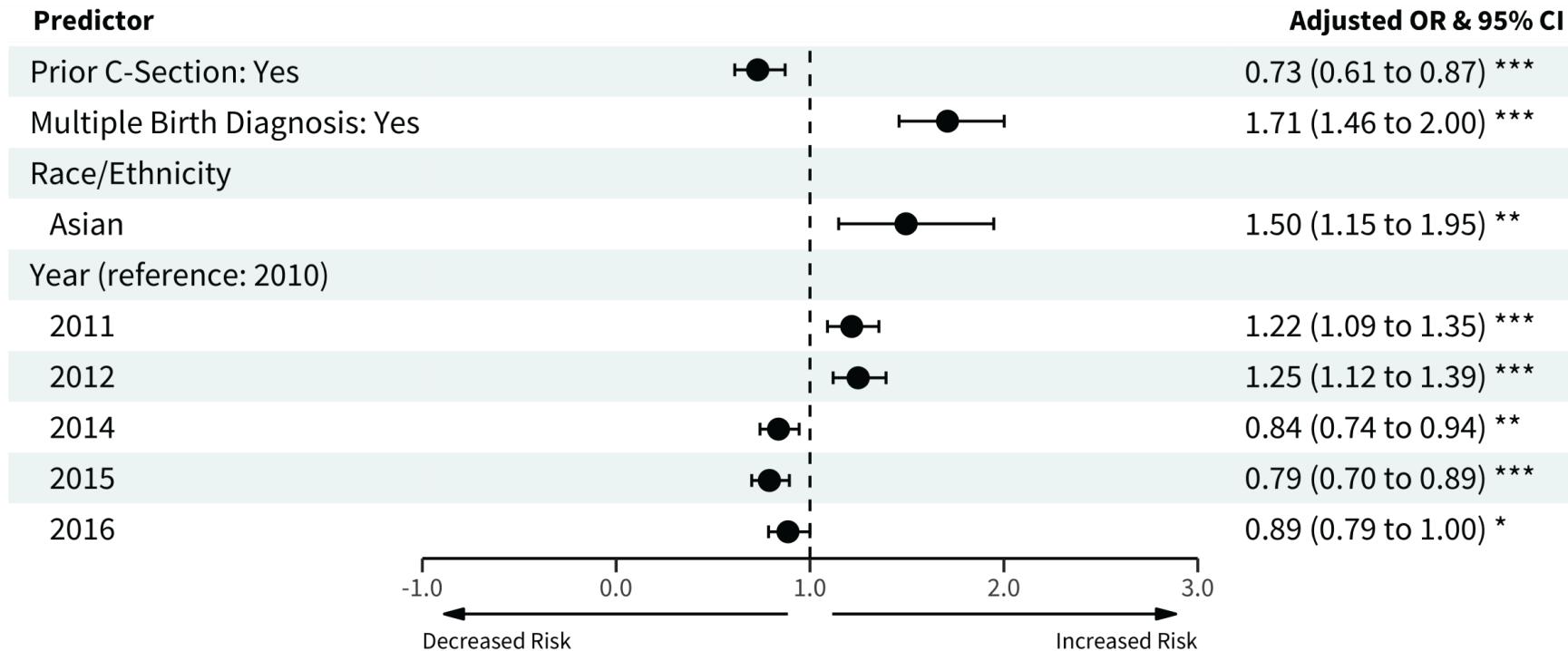


Hemorrhage: Rates over time



Hemorrhage: Model results

Hemorrhage: Adjusted odds ratio estimates with 95% confidence intervals



*p-value < 0.05, **p-value < 0.01, ***p-value < 0.001

Non-significant predictors: Sickle cell status, number of pain crisis before delivery; number of blood transfusions before delivery; delivery episode; patient age; blood type; blood Rh factor

Limitations

- The study did not include data on hemoglobin variants which would help
 - Confirm sickle cell status
 - Identify additional patients with homozygous sickle cell disease
 - Identify heterozygous patients that are asymptomatic
- Billing codes (e.g. ICD-9/10) are imperfect at capturing clinical conditions
- Blood transfusion capture after the transition to ICD-10 was limited by a change in coding practices [1]

1. [AIM Severe Maternal Morbidity \(SMM\) Data Alert for Blood Transfusions. 2016](#)

Conclusions

- Patients with sickle cell disease were not found to be at increased risk of hemorrhage, a severe maternal morbidity.
- Pregnancies of patients with sickle cell were at increased risk of blood transfusions and stillbirth.
- These results underscore the need for systemic support for comprehensive coordinated care for sickle cell patients, particularly during pregnancy and delivery

Publication

You'll be able to view the full results and read more about the study in our upcoming preprint.

🔗 Stay tuned for updates on the webpage for this talk:
The Impact of Sickle Cell Status on Adverse Delivery Outcomes Using Electronic Health Record Data



Thank you!

 silvia.rbind.io

 [@spcanelon](https://twitter.com/spcanelon)

 [@spcanelon](https://github.com/spcanelon)

This presentation was made using the
AMIA template and the following R packages:
[xaringan](#), [xaringanExtra](#), [kableExtra](#), and [forester](#).

Tables of significant model results

Stillbirth	Blood transfusion	Hemorrhage
Predictor	Adjusted OR & 95% CI	
Sickle Cell Status		
Sickle Cell Trait		8.94 (1.05 to 75.79) *
Sickle Cell Disease		26.40 (2.48 to >100) **
Prior C-Section: Yes		0.44 (0.22 to 0.78) **
Multiple Birth Diagnosis: Yes		4.68 (3.48 to 6.29) ***
Marital Status: Married		0.72 (0.57 to 0.91) **
Race/Ethnicity		
Black/African American × Sickle Cell		0.11 (0.01 to 0.93) *

* pvalue < 0.05, ** p-value < 0.01, *** p-value < 0.001

Tables of significant model results

	Stillbirth	Blood transfusion	Hemorrhage
Predictor	Adjusted OR & 95% CI		
Sickle Cell Status			
Sickle Cell Disease	47.07 (5.33 to >100) ***		
Number of Pain Crises Before Delivery	0.90 (0.82 to 0.99) *		
Number of Blood Tranfusions Before Delivery	1.70 (1.28 to 2.27) ***		
Prior C-Section: Yes	2.58 (1.87 to 3.56) ***		
Delivery Episode	0.64 (0.53 to 0.79) ***		
Multiple Birth Diagnosis: Yes	2.91 (2.24 to 3.77) ***		
Patient Age	1.02 (1.01 to 1.03) **		
Race/Ethnicity			
Asian	1.89 (1.01 to 3.52) *		
Blood Type (reference: Blood Type O)			
Blood Type A	1.16 (1.00 to 1.34) *		
Blood Rh Factor (reference: Rh Positive)			
Rh Negative	1.27 (1.03 to 1.57) *		
Year (reference: 2010)			
2013	1.43 (1.14 to 1.79) **		
2014	1.34 (1.07 to 1.68) *		
2016	0.01 (0.00 to 0.05) ***		
2017	0.06 (0.02 to 0.17) ***		

* pvalue < 0.05, ** p-value < 0.01, *** p-value < 0.001

Tables of significant model results

Stillbirth	Blood transfusion	Hemorrhage
Predictor	Adjusted OR & 95% CI	
Prior C-Section: Yes	0.73 (0.61 to 0.87) ***	
Multiple Birth Diagnosis: Yes	1.71 (1.46 to 2.00) ***	
Race/Ethnicity		
Asian	1.50 (1.15 to 1.95) **	
Year (reference: 2010)		
2011	1.22 (1.09 to 1.35) ***	
2012	1.25 (1.12 to 1.39) ***	
2014	0.84 (0.74 to 0.94) **	
2015	0.79 (0.70 to 0.89) ***	
2016	0.89 (0.79 to 1.00) *	

* pvalue < 0.05, ** p-value < 0.01, *** p-value < 0.001