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

S17: Applied Clinical Research Informatics

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# About me

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

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# Learning objectives

Understand how electronic health record (**EHR**) data was 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 o. en 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

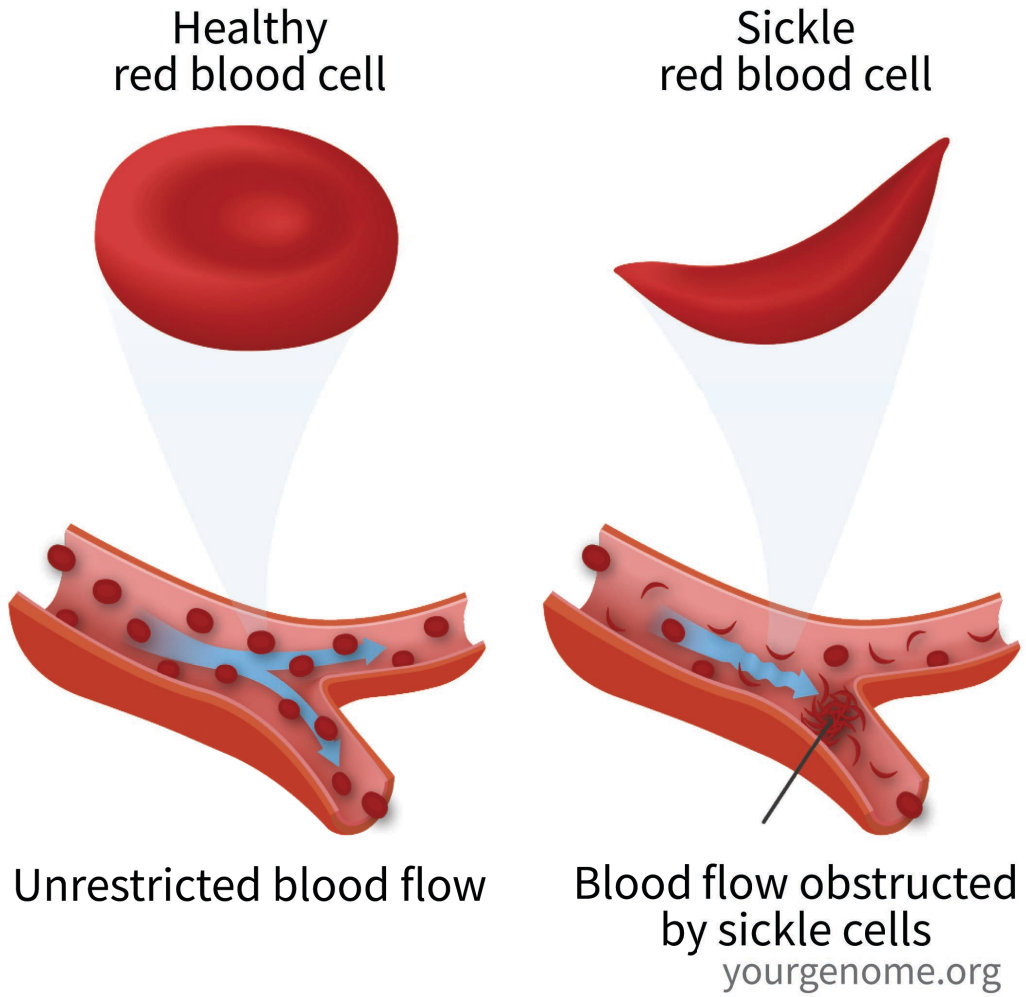
# Analysis

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)

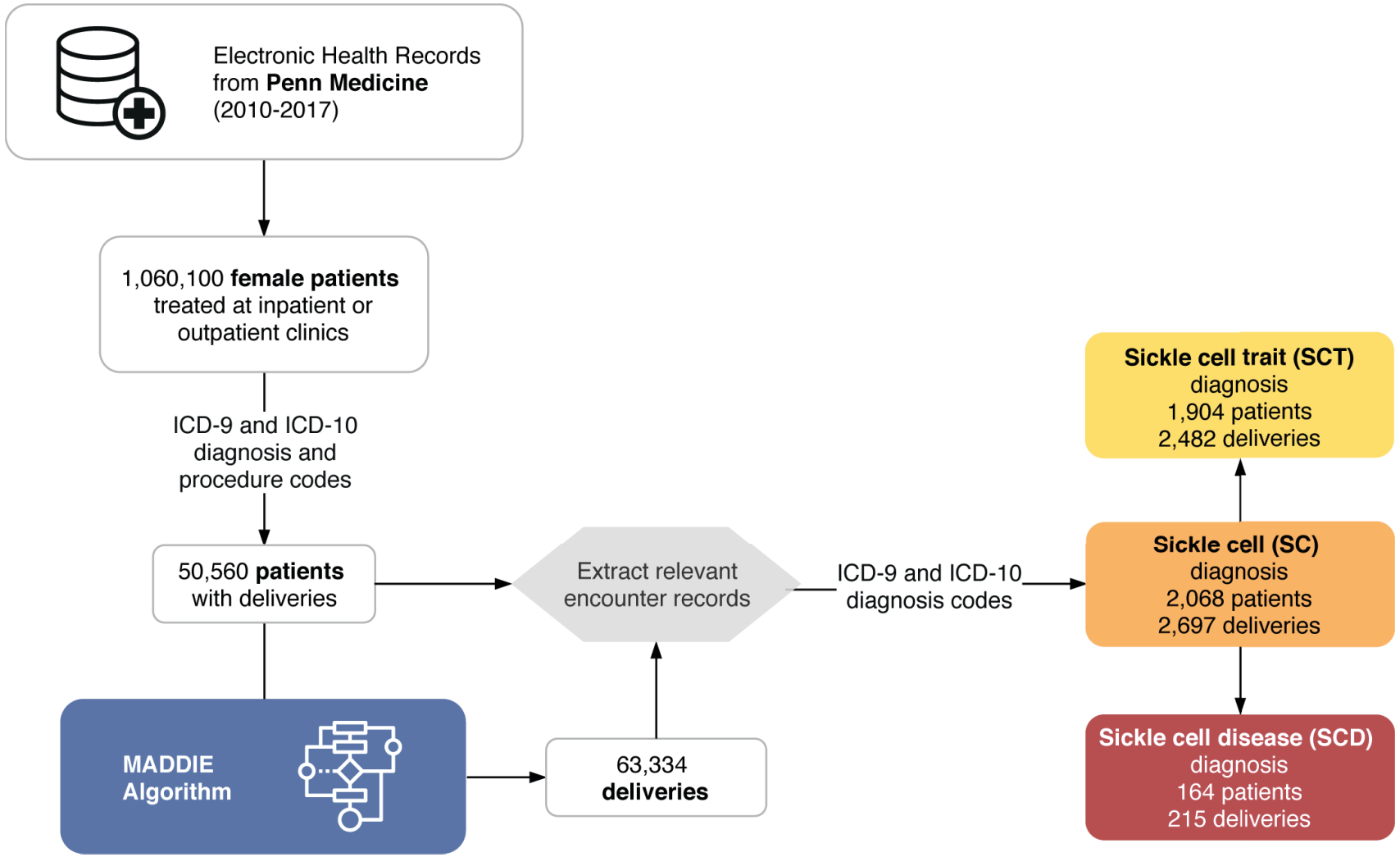
# Sickle cell disease

- Complex inherited genetic disorder and most common hemoglobinopathy in the U.S., a. ecting ~100,000 people [1]
- 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
- Primarily affects individuals of African ancestry and is associated with high lifetime morbidity and premature mortality [2]

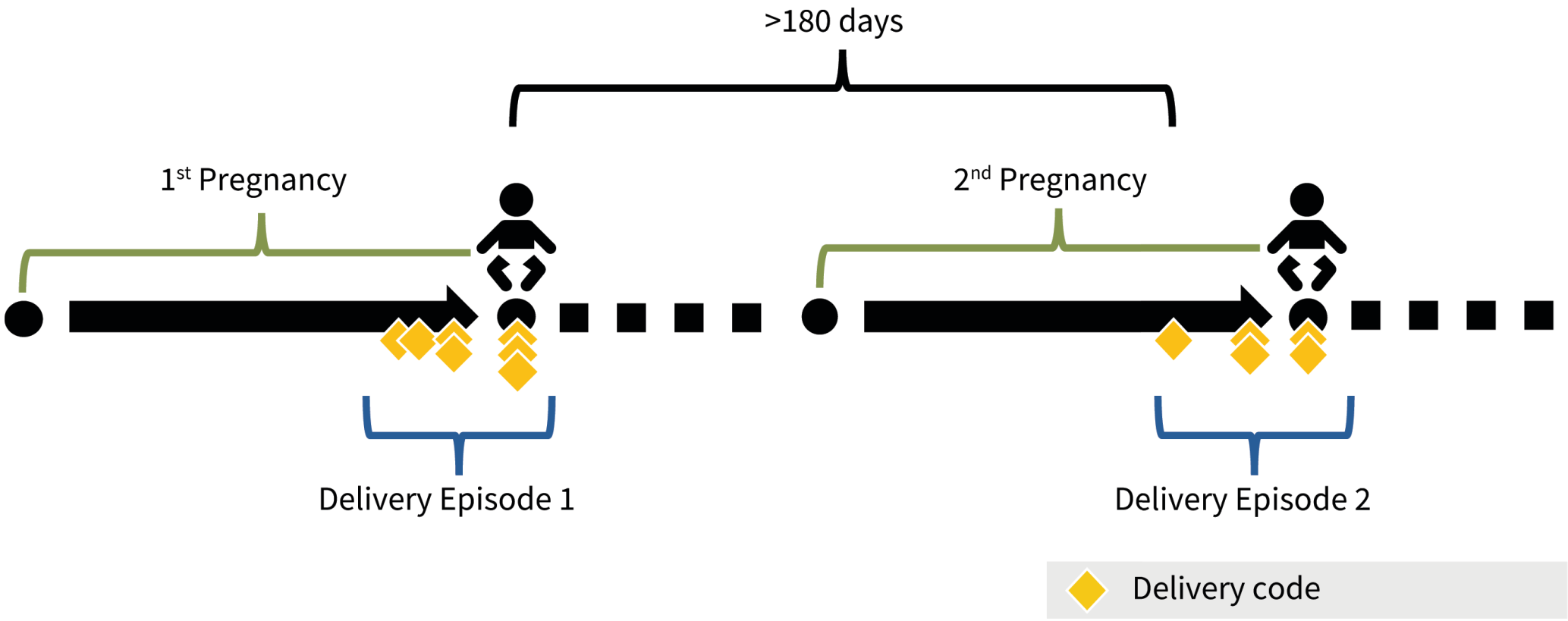



1. Centers for Disease Control and Prevention. Data & Statistics on Sickle Cell Disease. 2017
2. Kuo K, Caughey AB. Am J Obstet Gynecol. 2016;215(4)

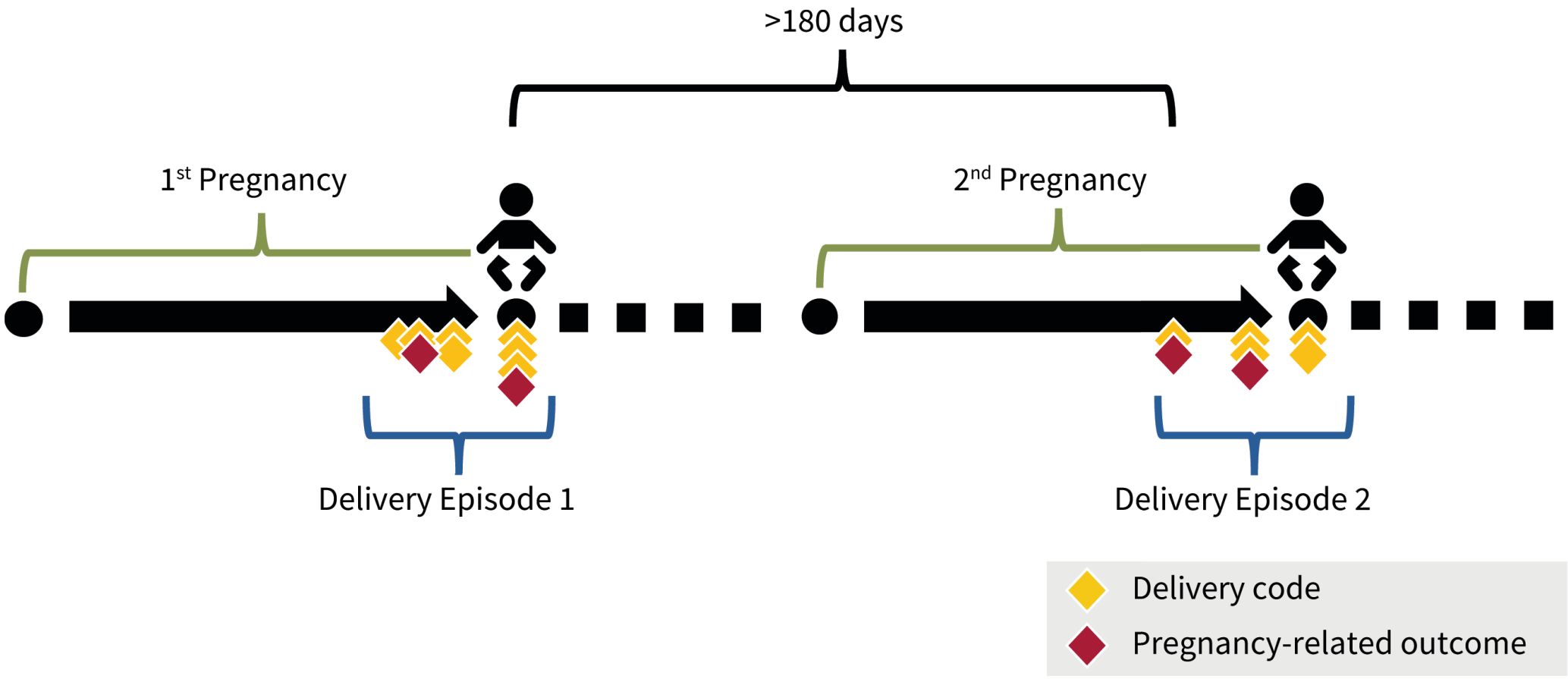
# Study overview



# 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 factor Rh
- Year

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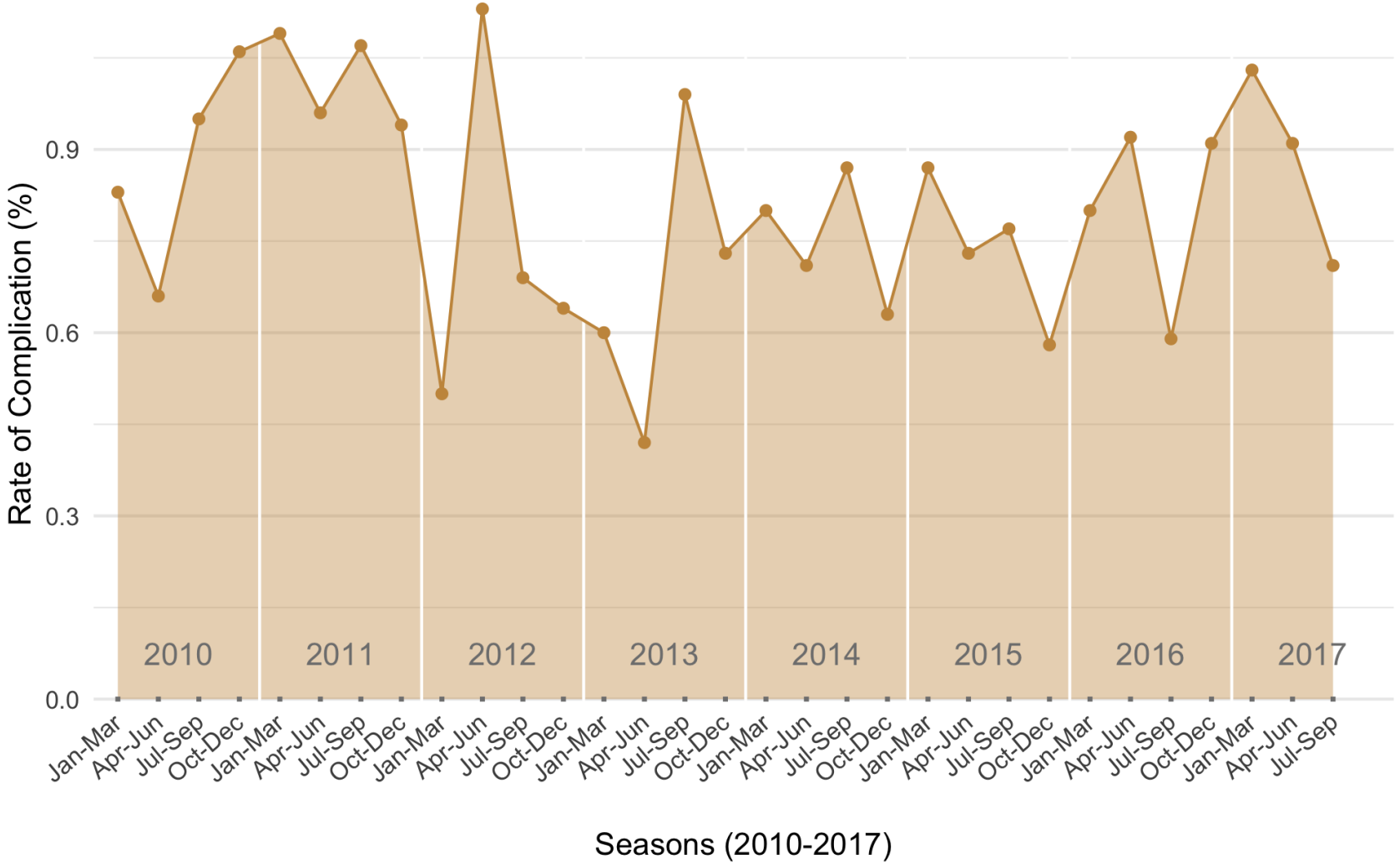
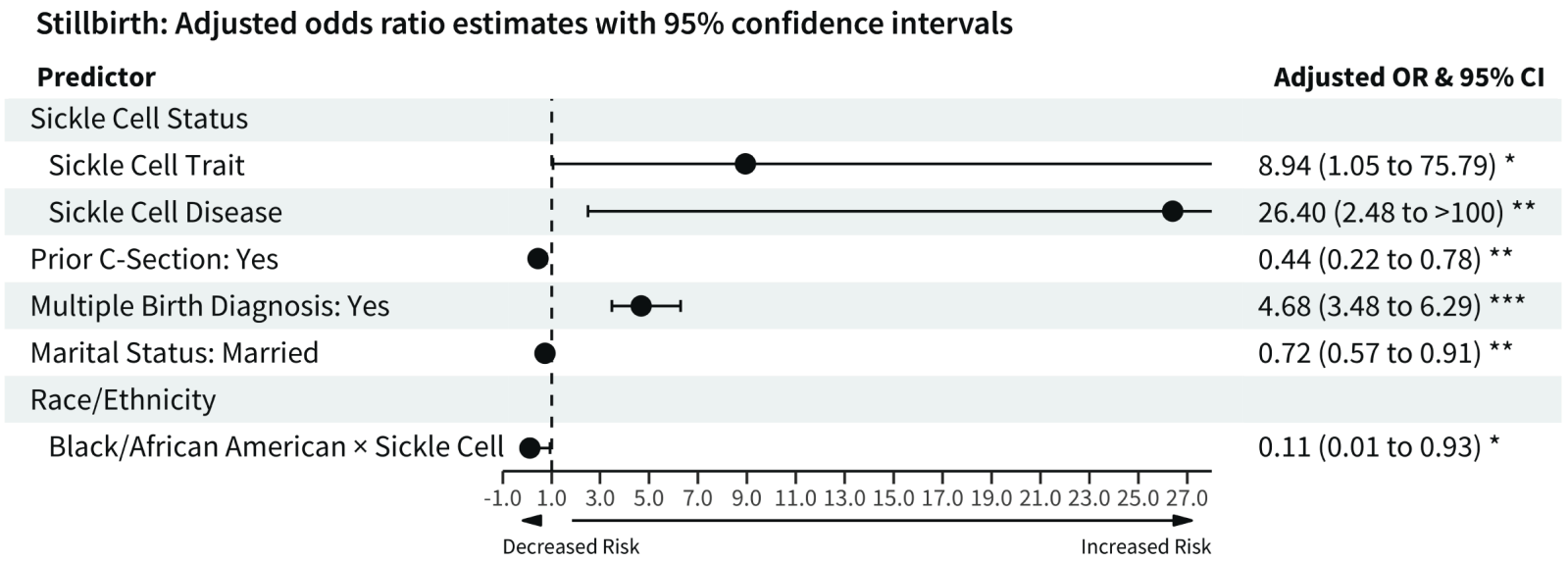
# Stillbirth: Rates over time

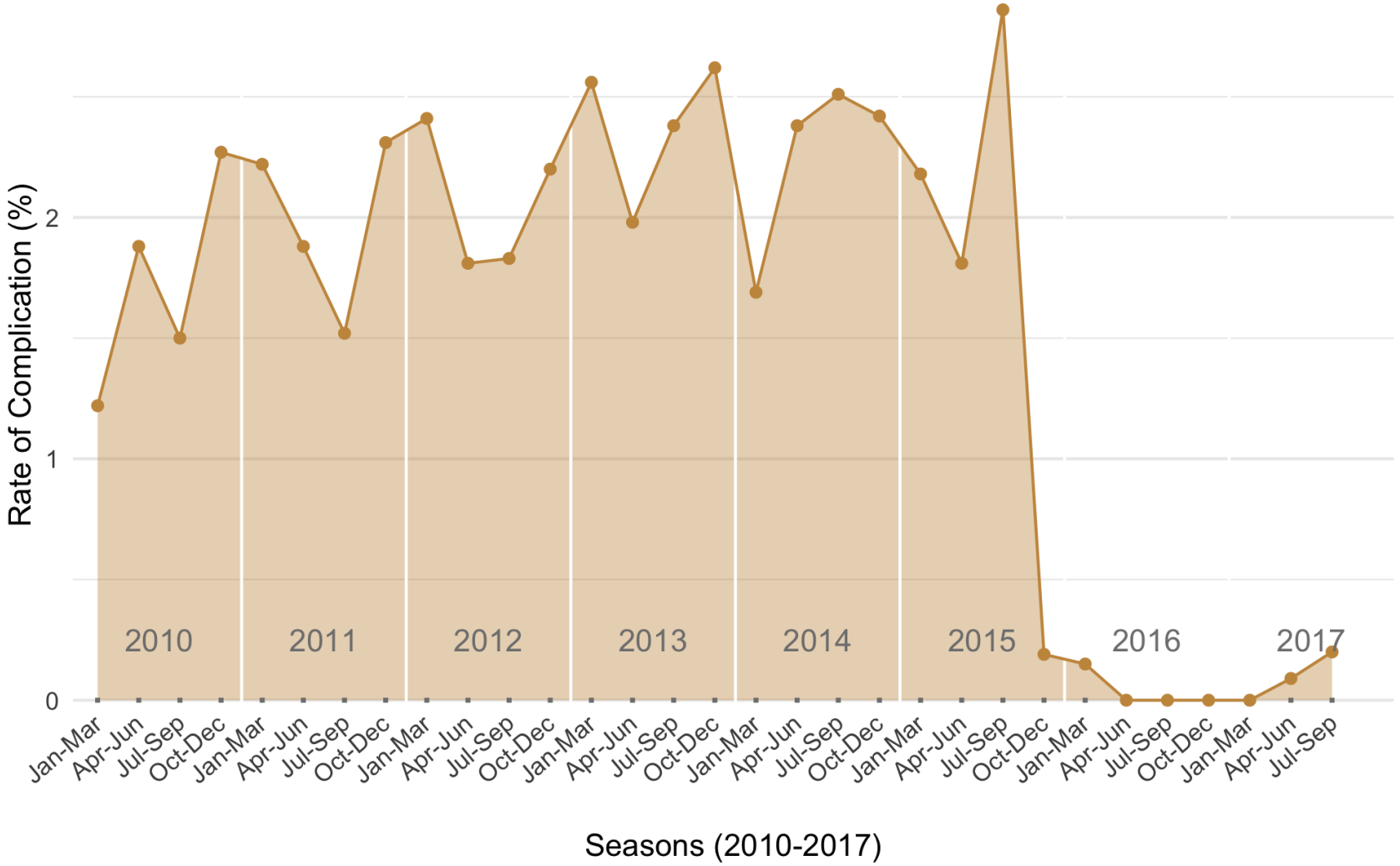


# Stillbirth: Model results




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

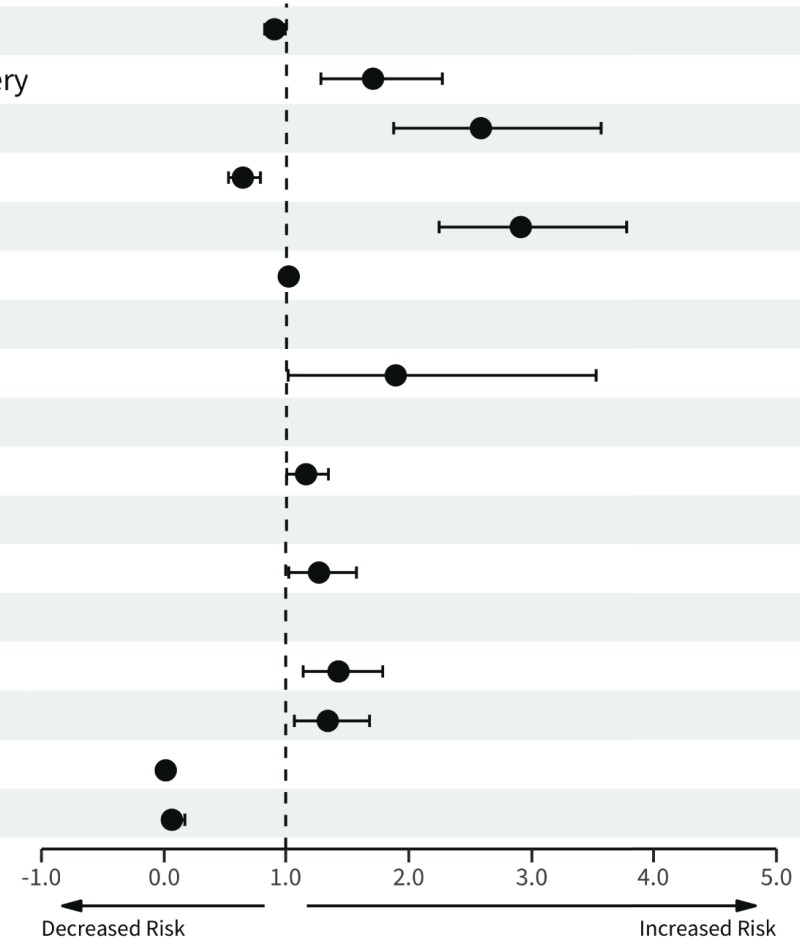
# Blood transfusion: Rates over time



# Blood transfusion: Model results

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

| Predictor | Adjusted OR & 95% CI |
|---|---|
| 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 Factor Rh (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) *** |

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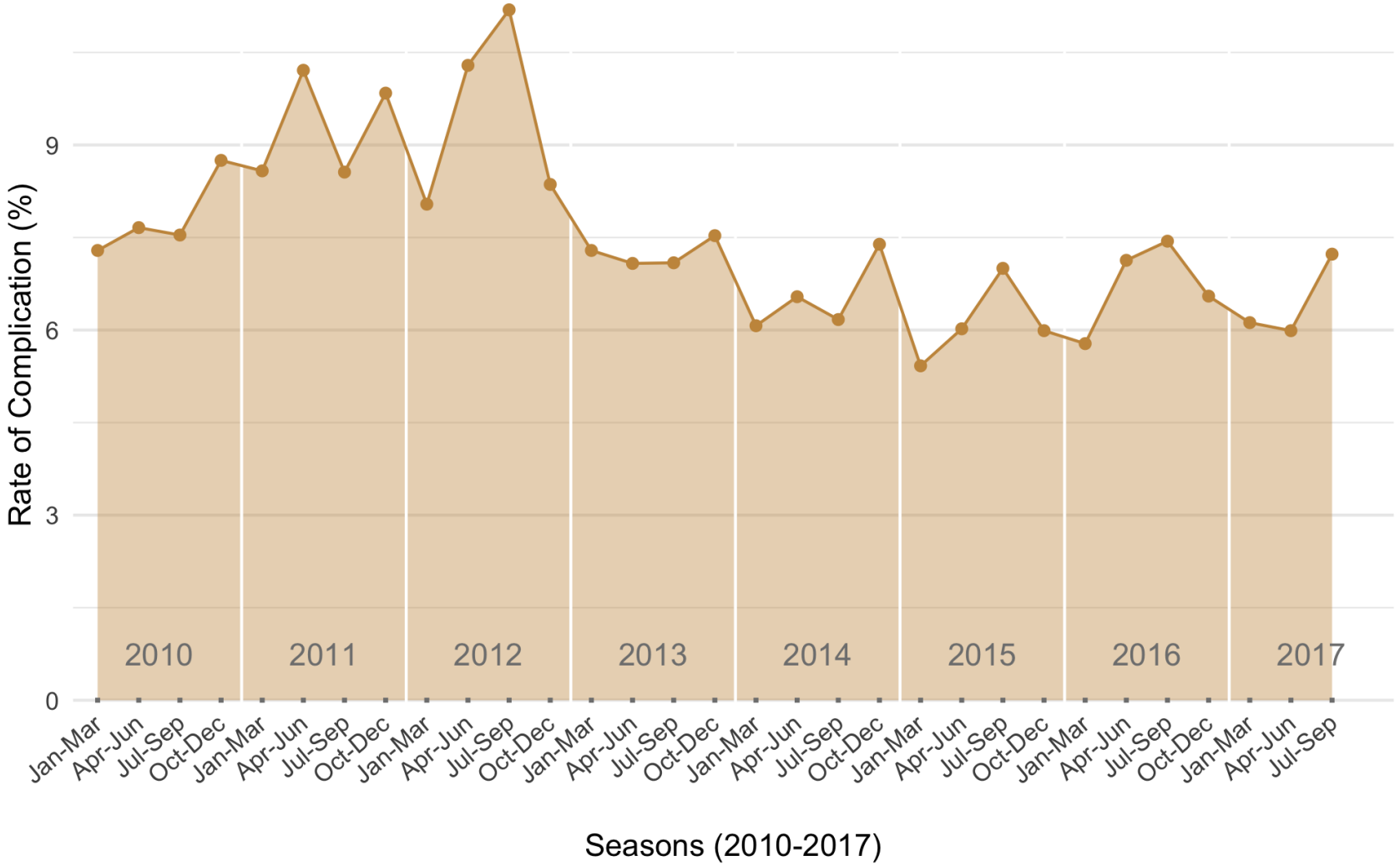
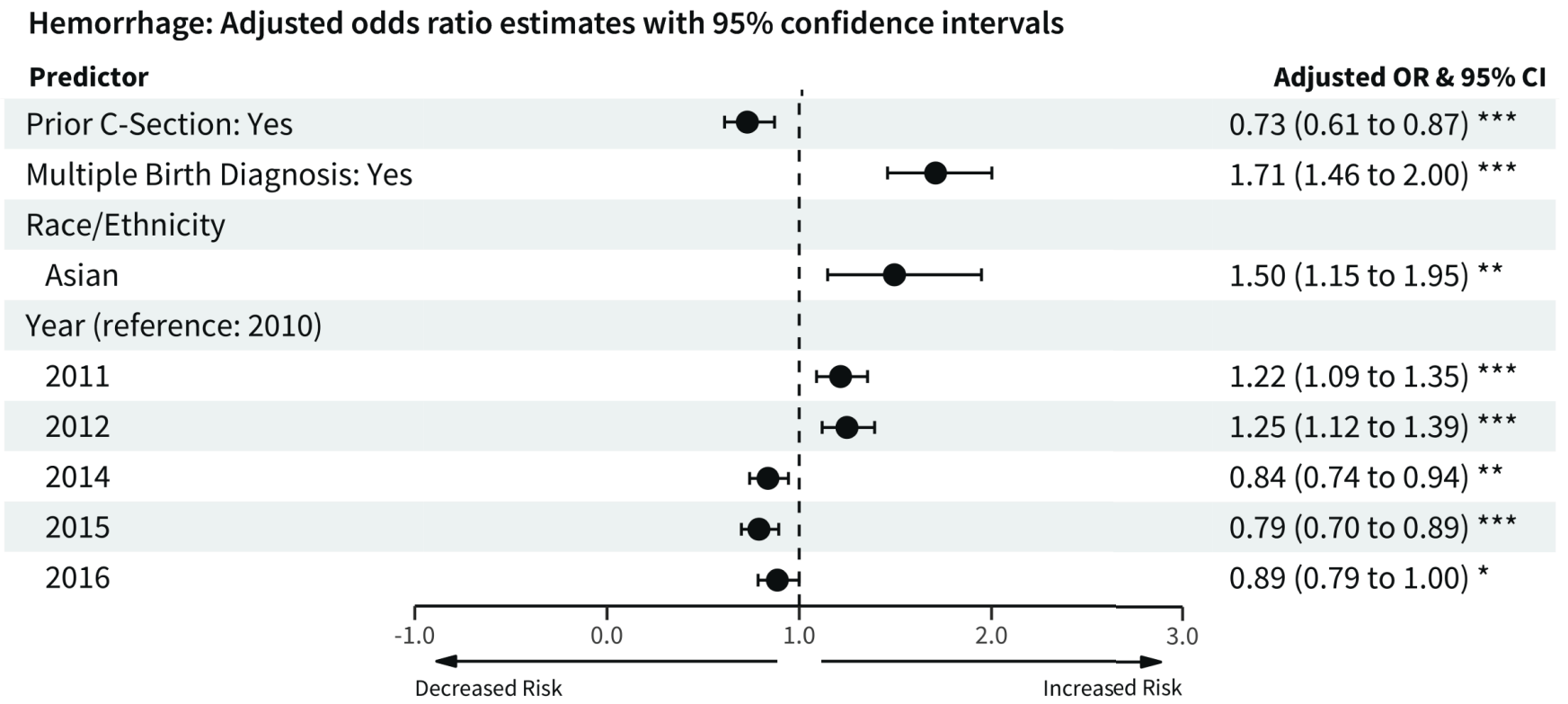
# Hemorrhage: Rates over time



# Hemorrhage: Model results

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# Limitations

- Billing codes (e.g. ICD-9/10) are imperfect at capturing clinical conditions
- 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
- 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 *all* adverse delivery outcomes, including 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

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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) *** |

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|---|---|
| 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