

Maternal Health Before and After Stillbirth

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Stillbirth Summit
Star Legacy Foundation
June 2021

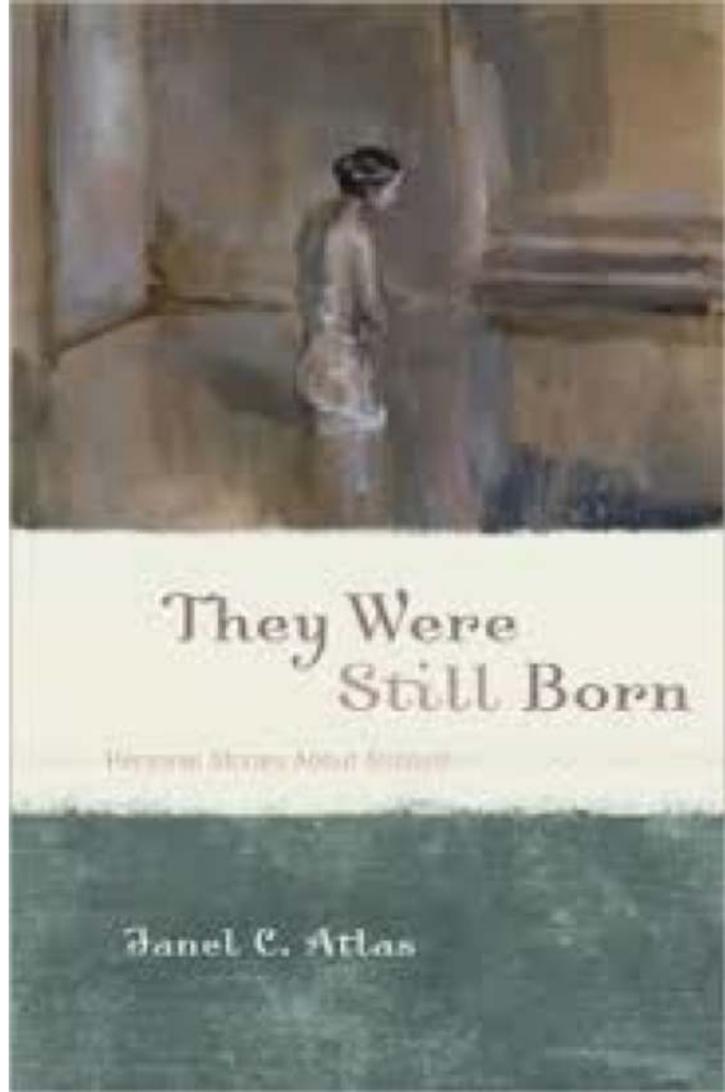
Outline

1. Overview of stillbirth prevalence and trends
 2. Maternal health → stillbirth
 3. Stillbirth → maternal health
- + *research challenges***



Stillbirth

Definition for purpose of this talk is an infant who was born at ≥ 20 weeks gestation and who died *in utero*



Stillbirth: As common as infant death

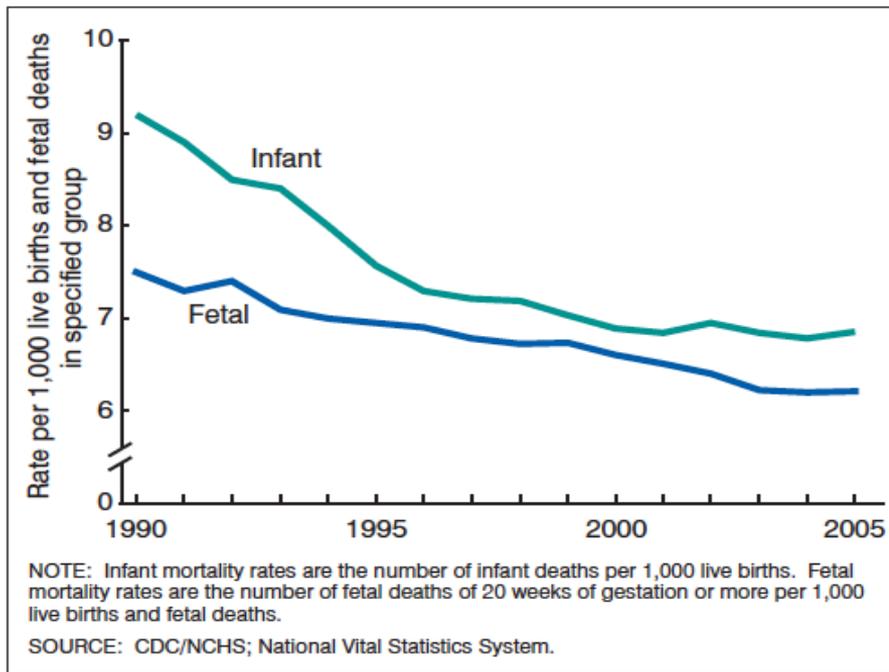


Figure 2. Fetal and infant mortality rates: United States, 1990–2005

Stillbirth: Early stillbirths haven't declined

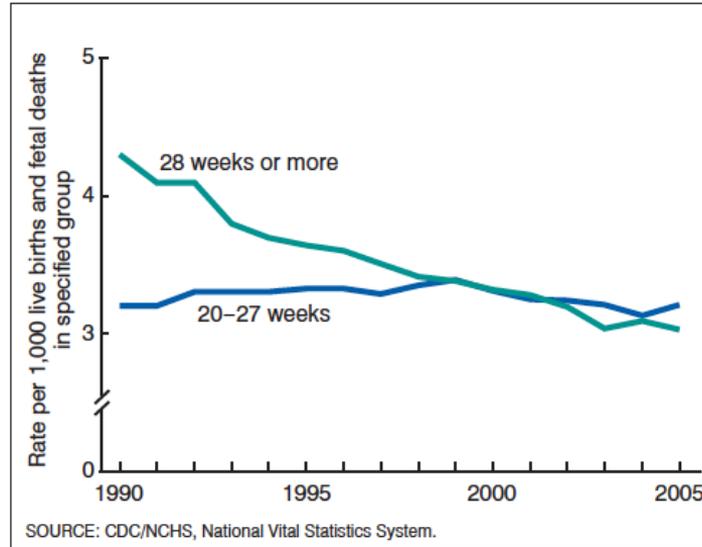


Figure 1. Fetal mortality rates by period of gestation: United States, 1990–2005

Gestational age distribution for stillbirths vs. live births.

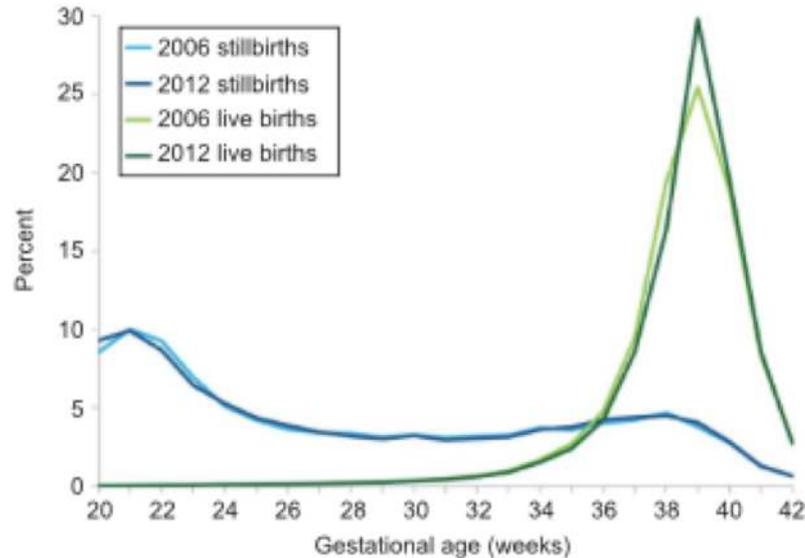
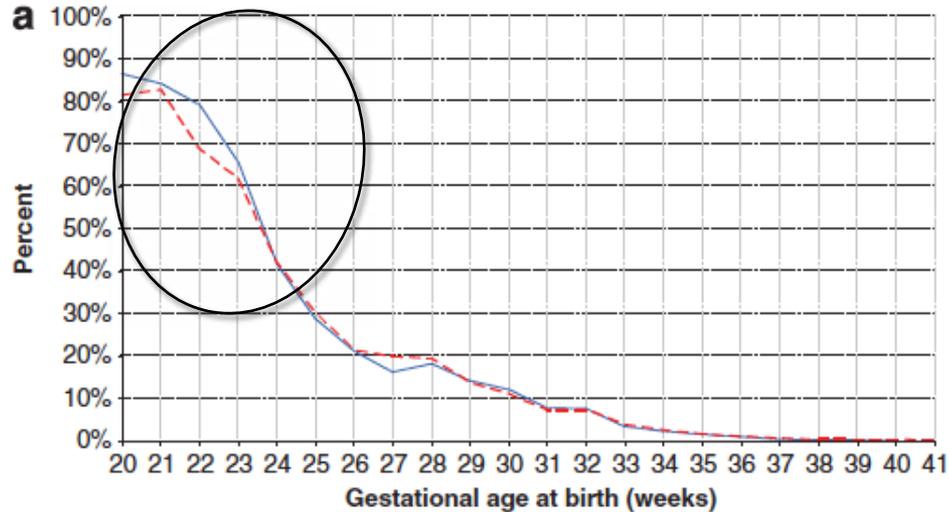


Fig. 1. Percent distribution of stillbirths and live births by gestational age, United States, 2006 and 2012. Data from the Centers for Disease Control and Prevention/National Center for Health Statistics, National Vital Statistics System. MacDorman. *Trends in Stillbirth by Gestational Age.* *Obstet Gynecol* 2015.

Stillbirth: Majority of early births are stillbirths Majority of stillbirths occur at <28 wks



Percentage of stillbirths among all live births and stillbirths.
(Singletons only; Males – solid blue line; females – dashed red line)

“Perivable” Births (20-25 wks)

++ Interest due to low survival & high morbidity among survivors, and questions about clinical management

NIH PA-15-200 “Studies at Perivable Gestation”

→ Address issues of care as well as causes

Stillborn babies are a critical component of all births at 20-25 weeks but usually excluded

Maternal Risk Factors for Stillbirth

Maternal Risk Factors for Stillbirth

Stillbirth and Live Birth at Periviable Gestational Age: A Comparison of Prevalence and Risk Factors



Am J Perinatol 2019;36:537-544.

Suzan L. Carmichael, PhD¹ Yair J. Blumenfeld, MD² Jonathan A. Mayo, MPH¹ Jochen Profit, MD¹
Gary M. Shaw, DrPH¹ Susan R. Hintz, MD¹ David K. Stevenson, MD¹

Association of Risk Factors with Stillbirth & Live Birth at 20-25 Wks

Variable	Fetal death	Live birth died<7d	Live birth surv. 7+d
Maternal age (years)	1.03 (1.03,1.04)	1.03 (1.02,1.04)	1.04 (1.03,1.04)
Maternal height (in.)	1.00 (0.99,1.01)	1.00 (0.98,1.02)	1.00 (0.98,1.01)
<u>Race-ethnicity: White</u>	ref	ref	ref
Black	2.3 (2.1,2.6)	3.6 (3.1,4.1)	3.5 (3.1,4.1)
Hispanic	1.0 (1.0,1.1)	1.4 (1.2,1.6)	1.5 (1.3,1.7)
<u>Education</u>			
<HS graduation	1.3 (1.2,1.4)	1.0 (0.9,1.1)	1.1 (1.0,1.2)
High school grad	ref	ref	ref
Some college	1.1 (1.0,1.2)	0.9 (0.8,1.0)	0.9 (0.8,1.0)
College grad +	0.6 (0.5,0.7)	0.5 (0.4,0.6)	0.5 (0.4,0.6)
<u>Parity: 1+</u>	1.6 (1.5,1.7)	2.0 (1.8,2.2)	2.1 (1.9,2.3)
0	ref	ref	ref
<u>BMI</u>			
Underweight	0.8 (0.7,1.0)	1.2 (0.9,1.5)	1.1 (0.9,1.4)
Normal	ref	ref	ref
Overweight	1.3 (1.2,1.4)	1.2 (1.1,1.4)	1.3 (1.2,1.5)
Obese I	1.5 (1.3,1.6)	1.7 (1.5,2.0)	1.6 (1.4,1.8)
Obese II	1.9 (1.7,2.2)	1.9 (1.6,2.3)	2.0 (1.7,2.4)
Obese III	2.2 (1.9,2.5)	2.1 (1.7,2.6)	2.2 (1.8,2.6)
<u>Smoking: None</u>	ref	ref	ref
Any	1.8 (1.5,2.1)	1.6 (1.31,2.1)	1.8 (1.5,2.2)
<u>Prepreg HTN: No</u>	ref	ref	ref
Yes	2.8 (2.1,3.6)	1.7 (1.0,2.6)	1.9 (1.3,2.7)
<u>Prepreg Diabetes: No</u>	ref	ref	ref
Yes	2.3 (1.7,3.1)	0.9 (0.4,1.7)	1.6 (1.0,2.4)

- Table shows Adjusted Odds Ratios (95% CIs)
- **Reference** = live births born at term (37+ wks)

Conclusion

Inclusion of stillborn and liveborn babies in studies of deliveries at periviable gestations is important.

In order to understand preterm (live) birth, we need to understand stillbirth.

Maternal Risk Factors for Stillbirth

Maternal Risk Factors for Stillbirth

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

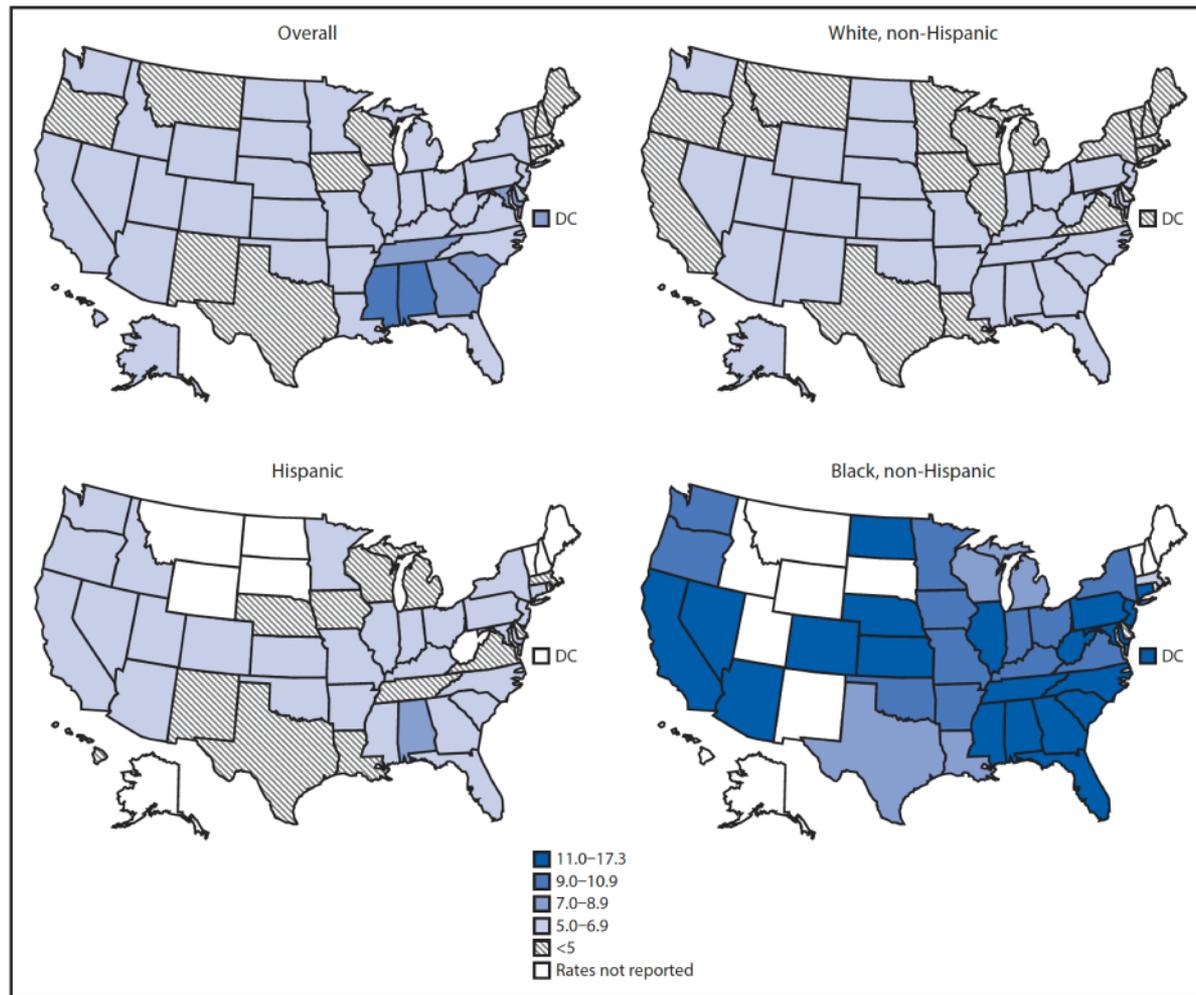
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September 18, 2020

Racial and Ethnic Disparities in Fetal Deaths — United States, 2015–2017

Shannon M. Pruitt, MPH^{1,2}; Donna L. Hoyert, PhD³; Kayla N. Anderson, PhD¹; Joyce Martin, MPH³; Lisa Waddell, MD⁴; Charles Duke, MD¹;
Margaret A. Honein, PhD¹; Jennita Reefhuis, PhD¹

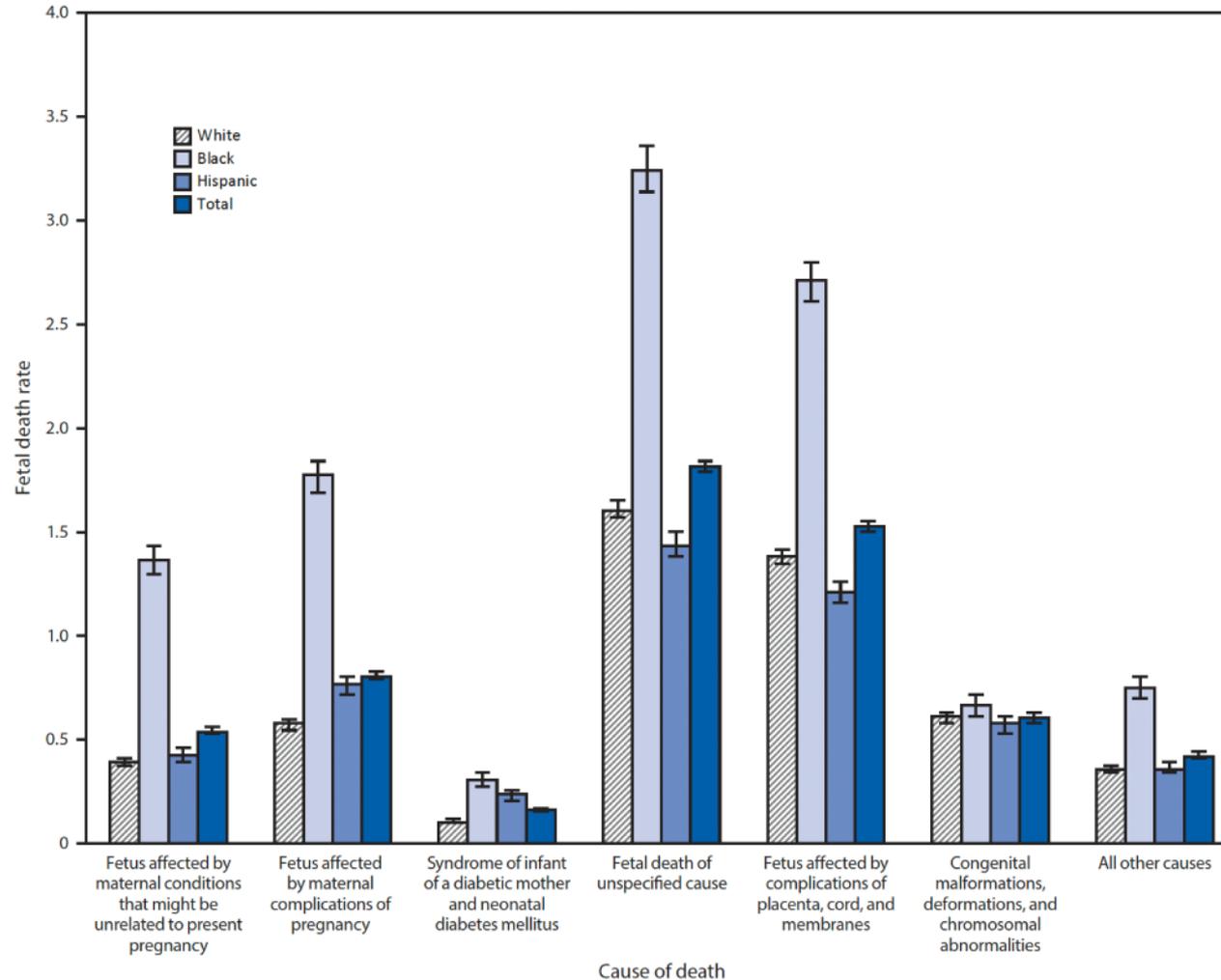
FIGURE 2. Fetal mortality rates, by states*† — United States, 2015–2017



Persistent racial/ethnic disparities

We need to understand social determinants, from social disadvantage to inequities in the health care system (access, quality), and how these lead to physiologic vulnerability

FIGURE 3. Fetal mortality rates,* by cause of death categories and maternal race/ethnicity† among states where >50% of fetal deaths had a documented cause^{5,¶} — United States,** 2015–2017



Fetal mortality by cause of death & race/ethnicity:

Disparities exist by all causes

Many have unknown causes

Most causes are related to maternal health

Maternal Risk Factors for Stillbirth

Maternal Health at Delivery & Stillbirth

Maternal Health After Stillbirth



Why focus on California?

- $\approx 500,000$ births/year
- 1 in 8 US births
- Diverse in many ways
- Rich, unique data resources

CA-OSHPD Linked Birth Cohort Files:

- Vital records – live birth & fetal death certificates (20+ wks)
- Hospital discharge records – pregnancy through postpartum = *maternal health*
- Links births to same mom over time
- Residential address from vital record





Why focus on maternal health?

In the United States,

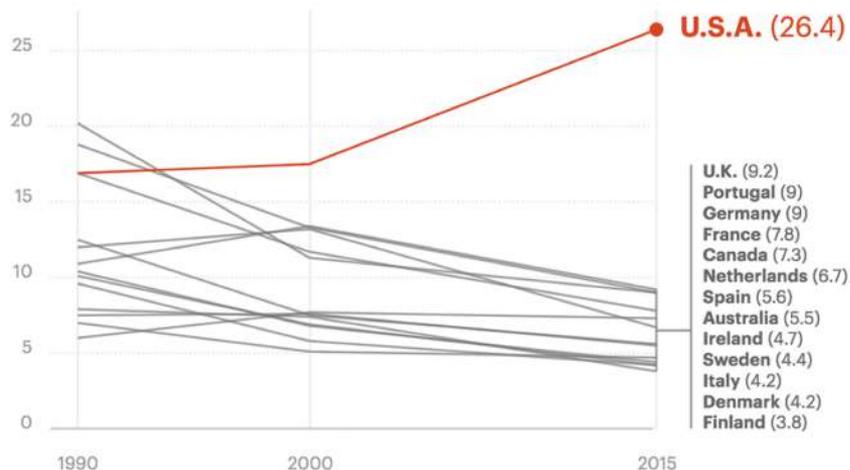
More women die from pregnancy and childbirth-related causes than any other developed country.

Maternal deaths are increasing.

Many deaths are considered preventable through better care.

Black & Indigenous American women are 2 to 4 times more likely to die than the rest of the population.

Deaths per 100,000 live births





Why study Severe Maternal Morbidity?

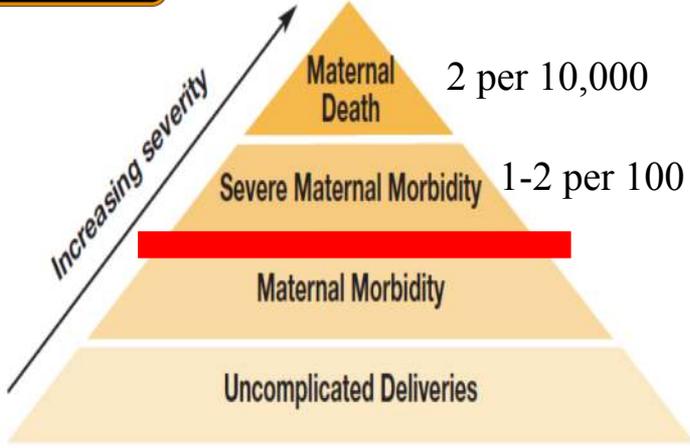


Figure 1. Continuum of Maternal Morbidity Showing Variation in Severity

From: NYC Dept of Health & Mental Hygiene. 2016. Severe Maternal Morbidity in NYC, 2008-12. NY, NY.

Maternal death is rare – SMM is more common

SMM precedes most maternal deaths

Composite of conditions that put women most at risk of death (CDC Index)

Similarities to maternal death:

- Increasing (doubled in last 2 decades)
- Racial-ethnic disparities
- High preventability
- Shared common causes – hemorrhage, cardiovascular events, hypertensive disorders, sepsis...

Maternal Health at Delivery, & Stillbirth

More hemorrhage, infection, peripartum hysterectomy*

* Gold KJ, Mozurkewich EL, Puder KS, Treadwell MC. Maternal complications associated with stillbirth delivery: A cross-sectional analysis. *J Obstet Gynaecol.* 2016;36(2):208-212.

Friedman AM, Wright JD, Ananth CV, Siddiq Z, D'Alton ME, Bateman BT. Population-based risk for peripartum hysterectomy during low- and moderate-risk delivery hospitalizations. *Am J Obstet Gynecol.* 2016;215(5):640.e641-640.e648.

Severe Maternal Morbidity Among Stillbirth and Live Birth Deliveries in California

Elizabeth Wall-Wieler, PhD, Suzan L. Carmichael, PhD, Ronald S. Gibbs, MD, Deirdre J. Lyell, MD, Anna I. Girsan, MD, PhD, Yasser Y. El-Sayed, MD, and Alexander J. Butwick, FRCA, MS

(Obstet Gynecol 2019;00:1–8)

Assess the prevalence and risk of severe maternal morbidity among delivery hospitalizations for stillbirth compared with live birth



Study Design

California births from 1999-2011

n=25,997 stillbirth, 6,433,845 live birth deliveries

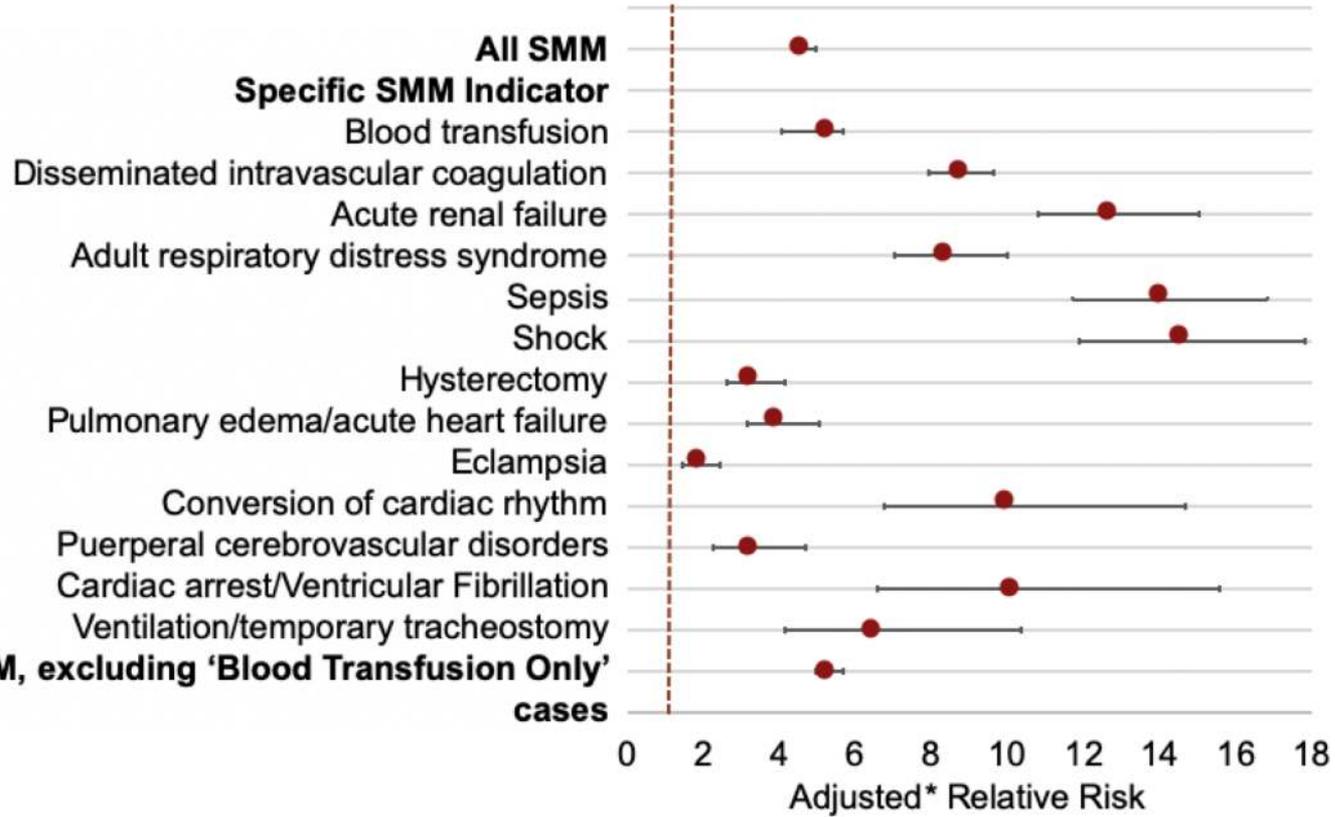
SMM based on CDC algorithm

Table 1. Prevalence of Severe Maternal Morbidity (SMM) and its Specific Indicators per 10,000 Delivery Hospitalization, Among Women with Stillbirth and Live Birth Deliveries

SMM	Stillbirths (n=25,997)	Live Births (n=6,433,845)
	SMM Cases (Prevalence*)	SMM Cases (Prevalence*)
All	1,503 (578)	63,819 (99)
Specific SMM Indicator		
Blood transfusion	1,080 (415)	41,233 (64)
Disseminated intravascular coagulation	402 (155)	9,818 (15)
Acute renal failure	169 (65)	1,820 (3)
Adult respiratory distress syndrome	143 (55)	2,791 (4)
Sepsis	137 (53)	1,863 (3)
Shock	110 (42)	1,515 (2)
Hysterectomy	82 (32)	5,175 (8)
Pulmonary edema/acute heart failure	74 (29)	2,745 (4)
Eclampsia	52 (20)	5,156 (8)
Conversion of cardiac rhythm	30 (12)	518 (1)
Puerperal cerebrovascular disorders	29 (11)	1,660 (3)
Cardiac arrest/Ventricular Fibrillation	25 (10)	377 (1)
Ventilation/temporary tracheostomy	20 (8)	446 (1)
All, excluding 'Blood Transfusion Only' cases	834 (321)	29,787 (46)

* Per 10,000 (live and still) births

Figure 1. Risk of Severe Maternal Morbidity and its Specific Indicators among Women with Stillbirths Relative to Women with Live Births



* Adjusted for maternal race/ethnicity, age at delivery, parity, payment type at delivery, education level, pre-existing diabetes, pre-existing hypertension, pre-eclampsia, gestational diabetes, gestational hypertension.

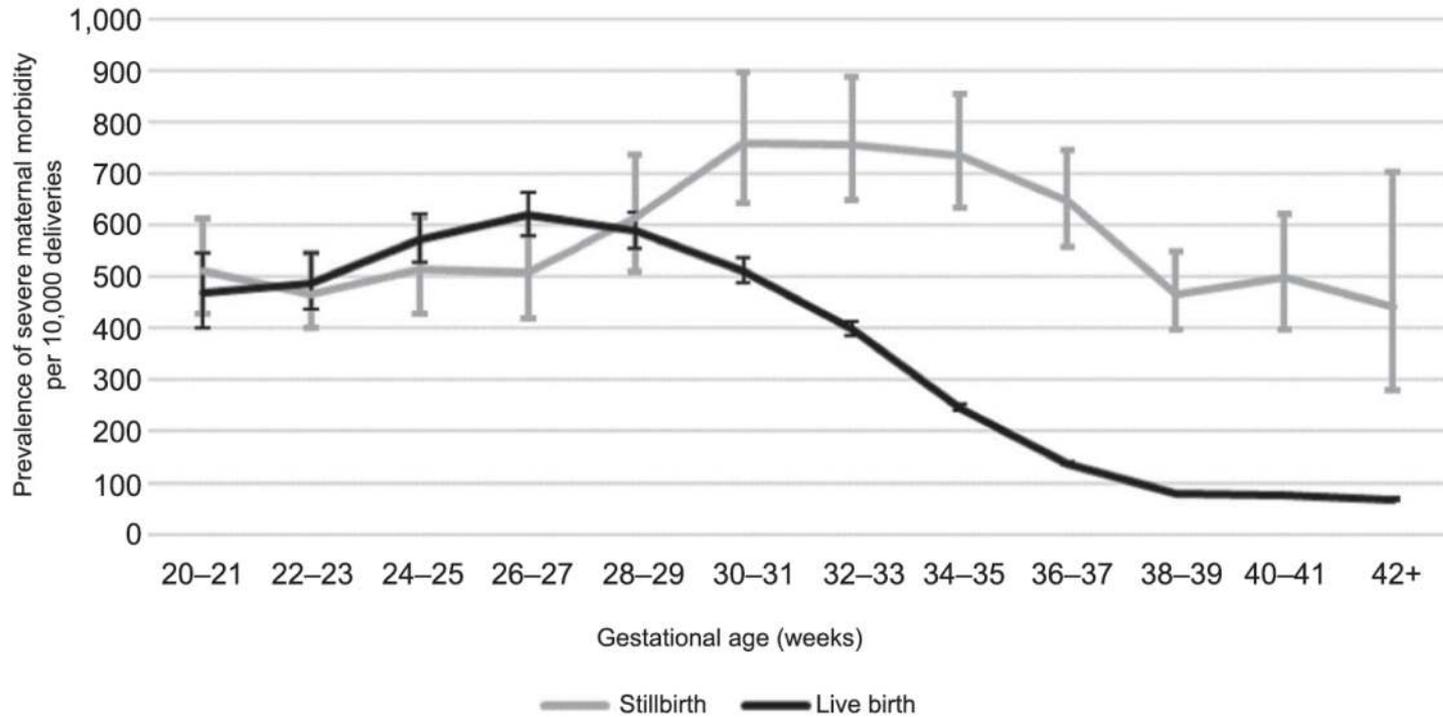
Table 2. Prevalence of Severe Maternal Morbidity (SMM) among Stillbirths by Cause of Fetal Death: California 1999 – 2011 (n = 25,997)

Cause of Fetal Death	Number (%) of Stillbirths	Number (%) of SMM Cases	SMM Prevalence per 10,000 stillbirths (95% CI)*
Hypertensive disorders	709 (2.7)	167 (11.1)	2355 (2024, 2741)
Placental conditions	3,111 (12.0)	596 (39.7)	1916 (1768, 2076)
Infections	661 (2.5)	60 (4.0)	908 (705, 1169)
Maternal medical conditions	608 (2.3)	51 (3.4)	839 (638, 1104)
Other	1840 (7.1)	98 (6.5)	533 (437, 649)
Obstetric complications	3920 (15.1)	164 (10.9)	418 (360, 486)
Missing	433 (1.7)	18 (1.2)	416 (262, 660)
Not Otherwise Specified	7,096 (27.3)	235 (15.6)	331 (291, 376)
Umbilical cord anomalies	4923 (18.9)	79 (5.3)	161 (129, 200)
Fetal major structural malformations and/or genetic abnormalities	2,696 (10.4)	35 (2.3)	130 (93, 181)

* Ranked from highest to lowest prevalence

Reference: 99 cases of SMM per 10,000 live births

Fig. 2. Prevalence of SMM per 10,000 births by gestational age, California, 1999-2011



Maternal Health After Stillbirth

Maternal Health After Stillbirth

Effects on mental health*

Understudied, underappreciated

* Burden C, Bradley S, Storey C, et al. From grief, guilt pain and stigma to hope and pride - a systematic review and meta-analysis of mixed-method research of the psychosocial impact of stillbirth. *BMC Pregnancy Childbirth*. 2016;16:9.

Hogue CJ, Parker CB, Willinger M, et al. The association of stillbirth with depressive symptoms 6-36 months post-delivery. *Paediatr Perinat Epidemiol*. 2015;29(2):131-143.

Postpartum Hospital Readmission

Hospital readmission receives attention in non-birth-related context, due to increasing trends and cost, and as a quality of care metric

Postpartum period is an understudied, vulnerable time

- In US, 30-day postpartum readmission rate is 1.0% (Clapp 2017 JAMA)
- In California, 1 in 12 women visited emergency department within 90 post-discharge (Batra 2017 Obstet Gynecol)
- 40% of women do not attend postpartum check-up

Find ways to prevent these events



Postpartum Hospital Readmission

(NICHD/NIH R03 HD095034)

Use data from 7 million births from 1998-2011 in California (1 in 8 US births) to:

Aim 1. Determine *incidence of and indications* for postpartum hospital readmission after delivery among women who had a stillbirth.

Aim 2. Identify *risk factors* for postpartum readmission among women who had a stillbirth.



Alex Butwick, MD, MS

Maternal Health after Stillbirth: Postpartum Hospital Readmission in California

Elizabeth Wall-Wieler, PhD¹ Alexander J. Butwick, FRCA, MS² Ronald S. Gibbs, MD³ 
Deirdre J. Lyell, MD³ Anna I. Girsen, MD, PhD³ Yasser Y. El-Sayed, MD³ Suzan L. Carmichael, PhD⁴

Assess whether risk of postpartum readmission within 6 weeks of giving birth differs for women who had stillbirths compared to live births

Examine whether diagnoses and procedures associated with postpartum readmission differed for women who had stillbirths compared to women who had live births



Study Design

California births, 1999 - 2011 (OSHPD) (n = 7,412,205)

N = 29,832 stillbirths

Readmission: Within 42 days of giving birth
(transfer \neq readmission)

Diagnoses and Procedures: All listed in the first readmission; grouped into 17 diagnosis clusters, 4 procedure clusters

Results: Cumulative Percent of Women with Readmission

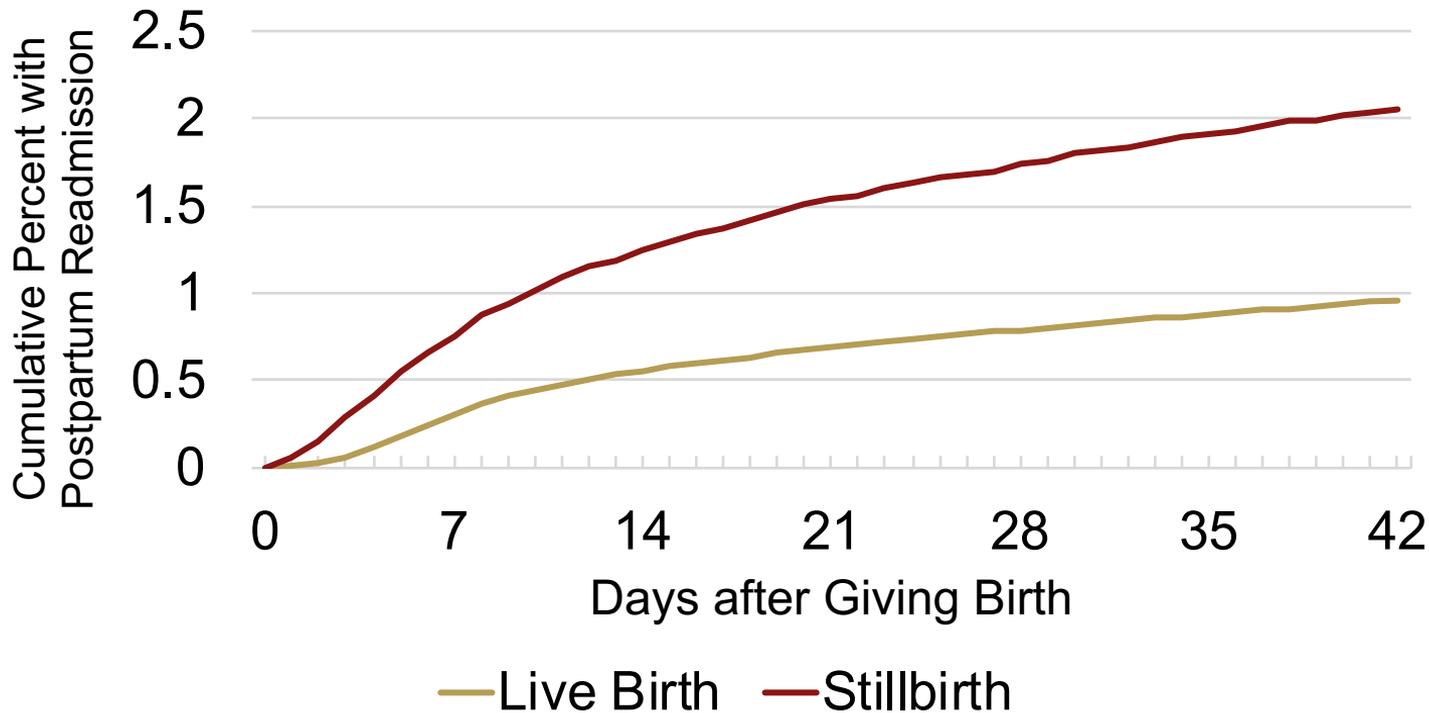


Table 2 Rate and relative risk of postpartum hospital readmission within 6 weeks of birth among women who had stillbirths versus live births, overall and by specific maternal diagnosis/procedure clusters at readmission; California, 1997 to 2011

Postpartum readmission	Stillbirth (n = 29,832)	Live birth (n = 7,368,808)	Relative risk (95% confidence interval)		
	n (rate ^a)	n (rate ^a)	Unadjusted	Model 1 ^b	Model 2 ^c
All	614 (206)	70,559 (96)	2.17 (2.01–2.36)	1.94 (1.79–2.10)	1.47 (1.35–1.60)
Specific diagnosis/ procedure clusters					
Uterine infection/pelvic inflammatory disease	142 (48)	13,435 (18)	2.61 (2.22–3.09)	2.45 (2.08–2.90)	1.79 (1.50–2.15)
Psychiatric condition	113 (38)	5,433 (7)	5.15 (4.28–6.21)	3.83 (3.17–4.62)	2.29 (1.86–2.82)
Hypertensive disorder	100 (34)	8,040 (11)	3.08 (2.53–3.75)	1.93 (1.58–2.35)	1.49 (1.20–1.84)
Urinary tract infection	88 (29)	9,433 (13)	2.31 (1.87–2.85)	2.01 (1.63–2.48)	1.51 (1.21–1.89)
Nonspecific postpartum diagnosis	79 (26)	13,495 (18)	1.44 (1.16–1.81)	1.25 (1.01–1.57)	1.06 (0.85–1.35)
Dilation and curettage	72 (24)	4,729 (6)	3.77 (2.98–4.76)	3.71 (2.94–4.69)	1.84 (1.41–2.42)
Hemorrhage and/or retained products of conception	68 (23)	6,436 (9)	2.61 (2.06–3.32)	2.52 (1.98–3.21)	1.31 (1.01–1.71)
Transfusion	57 (19)	3,813 (5)	3.70 (2.85–4.80)	3.11 (2.39–4.05)	1.64 (1.23–2.17)
Gallbladder disease	51 (17)	11,853 (16)	1.06 (0.81–1.40)	1.06 (0.80–1.40)	1.10 (0.82–1.46)
Thrombotic event	51 (17)	2,521 (3)	5.00 (3.79–6.60)	4.38 (3.31–5.79)	2.71 (2.00–3.68)
Wound infection and/or breakdown	49 (16)	10,025 (14)	1.21 (0.91–1.60)	0.97 (0.73–1.29)	1.17 (0.87–1.55)
Acute cardiovascular disease	19 (6)	2,029 (3)	2.31 (1.47–2.64)	1.50 (0.95–2.36)	1.59 (1.00–2.55)
Upper respiratory infection	19 (6)	1,813 (2)	2.59 (1.65–4.07)	1.89 (1.20–2.98)	1.54 (0.96–2.48)

Model 1 and 2 adjusted for:

^bAdjusted for maternal race/ethnicity, age at delivery, payment type at delivery, education level, parity, preexisting diabetes, and preexisting hypertension.

^cAdjusted for maternal race/ethnicity, age at delivery, payment type at delivery, education level, parity, preexisting diabetes, preexisting hypertension, multiple gestation, gestational age, gestational diabetes, gestational hypertension, preeclampsia, mode of delivery, severe maternal morbidity at delivery, and length of stay in hospital after birth.

Conclusions

After adjustment for confounders, women who have stillbirths are at 50% higher risk of postpartum readmissions within 6 weeks of giving birth than women who have live births.

Most common diagnoses and procedures at first readmission differ between women who have stillbirths and women who have live births.

Closer postpartum medical follow up is needed for women following stillbirth to reduce risk of readmission.

Risk factors for postpartum readmission among women after having a stillbirth

Julia D. DiTosto, MS; Can Liu, PhD; Elizabeth Wall-Wieler, PhD; Ronald S. Gibbs, MD; Anna I. Girsen, MD, PhD; Yasser Y. El-Sayed, MD; Alexander J. Butwick, FRCA, MS; Suzan L. Carmichael, PhD



Identify risk factors for postpartum hospital readmission among women after having a stillbirth, within 6 wks and 6-42 wks after discharge from birth hospitalization

Study Design

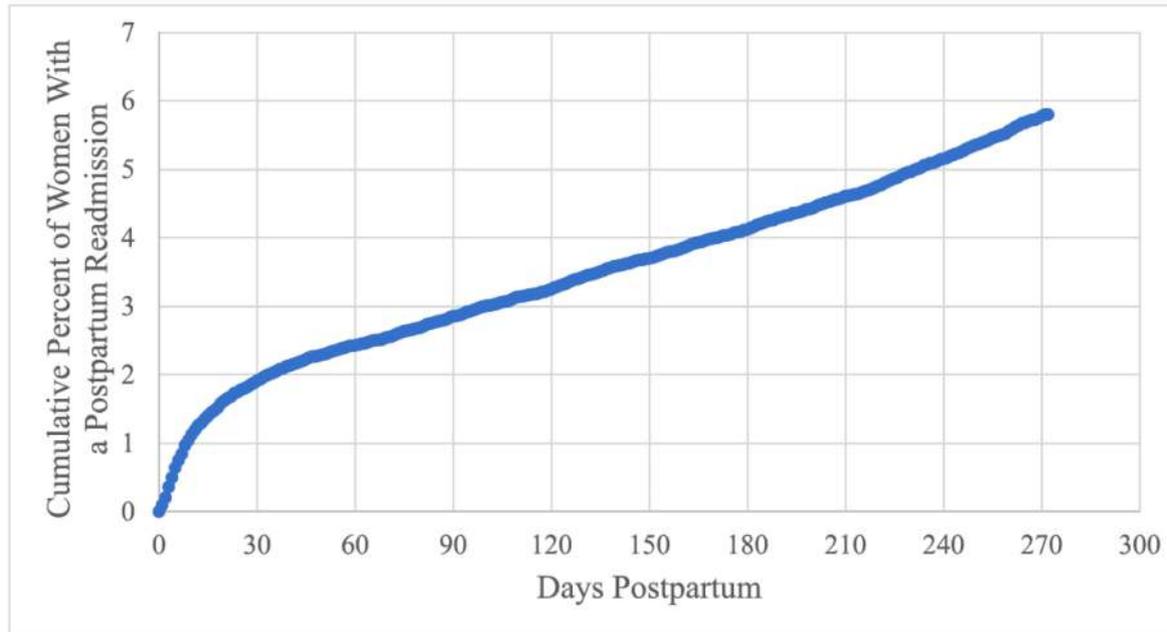
California births, 1999 - 2011 (OSHPD), n=29,654 stillbirths

Examined risk factors for readmission within 6 weeks and 6 weeks to 9 months after discharge from birth hospitalization

Models included sociodemographic, pre-pregnancy health-, pregnancy-, and birth-related variables

FIGURE 2

Cumulative percentage of postpartum readmission within 9 months after delivery among women who had a stillbirth in California, 1997–2011



DiTosto. Postpartum readmission after stillbirth. *Am J Obstet Gynecol MFM* 2021.

2.2% (n=642) readmitted within 6 wks (avg. 13.8 days)
5.8% readmitted within 9 months

	Odds Ratio		Odds Ratio	
	Unadjusted	Adjusted	Unadjusted	Adjusted
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sociodemographic^a				
Race/ ethnicity				
Non- Hispanic White	1.00 (ref)	1.00 (ref)		
Non- Hispanic Black	1.46 (1.16, 1.85)	1.38 (1.08, 1.76)		
Asian/ Pacific Islander	0.71 (0.52, 0.98)	0.87 (0.62, 1.23)		
Hispanic	0.81 (0.67, 0.98)	0.86 (0.69, 1.07)		
Other/ missing	1.85 (1.06, 3.53)	1.64 (0.91, 2.95)		
Age				
< 20	1.00 (0.75, 1.33)	0.94 (0.69, 1.27)		
20- 24	0.91 (0.71, 1.16)	0.86 (0.67, 1.10)		
25- 29	1.00 (ref)	1.00 (ref)		
30- 34	0.98 (0.78, 1.24)	1.01 (0.80, 1.28)		
35- 39	1.19 (0.93, 1.51)	1.23 (0.96, 1.58)		
>= 40	1.11 (0.78, 1.57)	1.16 (0.81, 1.65)		
Nativity				
US born	1.00 (ref)	1.00 (ref)		
Foreign born	0.70 (0.60, 0.83)	0.76 (0.62, 0.93)		
Education				
High school or less	1.24 (0.97, 1.59)	1.35 (1.02, 1.80)		
Some college	1.33 (1.01, 1.76)	1.31 (0.98, 1.75)		
Completed college	1.00 (ref)	1.00 (ref)		
Missing	1.73 (1.19, 2.52)	1.59 (1.05, 2.34)		
Payer				
Private	1.00 (ref)	1.00 (ref)		
Public/ government	1.04 (0.88, 1.23)	1.08 (0.89, 1.30)		
Other/ uninsured	1.09 (0.72, 1.64)	1.13 (0.74, 1.72)		
Missing	1.55 (1.12, 2.17)	1.50 (1.06, 2.11)		
Parity				
Nulliparous	1.00 (ref)	1.00 (ref)		
Parous	0.81 (0.69, 0.96)	0.86 (0.72, 1.03)		
			Pre- pregnancy health- related variables^b	
			Pre- pregnancy hypertension	2.23 (1.71, 2.90) 1.80 (1.36, 2.37)
			Pre- pregnancy diabetes	2.02 (1.53, 2.68) 1.78 (1.33, 2.37)
			Pregnancy- related variables^c	
			Gestational hypertension or preeclampsia	2.28 (1.84, 2.82) 1.93 (1.54, 2.42)
			Gestational diabetes	1.09 (0.78, 1.53) 0.82 (0.58, 1.18)
			Antenatal Hospitalization	2.14 (1.74, 2.65) 1.78 (1.43, 2.21)
			Birth- related variables^d	
			Mode of delivery	
			Vaginal	1.00 (ref) 1.00 (ref)
			Cesarean	1.82 (1.52, 2.17) 1.64 (1.36, 1.97)
			SMM at delivery ^e	
			Transfusion only	2.33 (1.63, 3.34) 1.95 (1.35, 2.81)
			Other SMM	3.89 (2.98, 5.09) 3.02 (2.28, 4.00)
			No SMM	1.00 (ref) 1.00 (ref)
			Gestational age	
			< 28 weeks	1.12 (0.90, 1.40) 1.10 (0.87, 1.37)
			28-31 weeks	1.40 (1.07, 1.80) 1.26 (0.97, 1.65)
			32-36 weeks	1.15 (0.90, 1.47) 1.05 (0.82, 1.35)
			37-40 weeks	1.00 (ref) 1.00 (ref)
			41+ weeks	1.41 (0.94, 2.11) 1.45 (0.96, 2.18)
			Birth hospitalization length of stay ^{**}	
			Normal	1.00 (ref) 1.00 (ref)
			Long	1.87 (1.58, 2.20) 1.59 (1.33, 1.89)
			Placental abruption	1.62 (1.32, 2.00) 1.42 (1.14, 1.76)
			Chorioamnionitis	0.87 (0.66, 1.15) 0.87 (0.66, 1.15)
			Hospital- related variables^e	
			Births per year	
			Less than 500	1.42 (0.90, 2.25) 1.32 (0.83, 2.10)
			500- 2000	1.02 (0.84, 1.23) 1.00 (0.83, 1.21)
			2000- 4000	1.00 (ref) 1.00 (ref)
			Greater than 4000	1.01 (0.83, 1.23) 0.98 (0.80, 1.19)

Conclusions

Similar pattern of results for 6 wk – 9 mo time period

Non-Hispanic black race/ethnicity, lower education, comorbidities, and birth-related complications associated with increased odds of postpartum readmission after having a stillborn baby, highlighting the importance of continued care for these women after the birth hospitalization

Maternal health matters!

Thank you!

This work was supported by NIH (NR017020
and HD095034)

We make the road by walking.

- *Antonio Machado*

