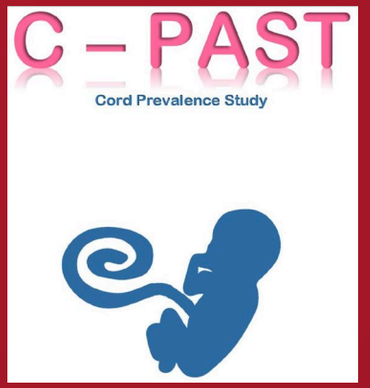
Let's talk about substance use, overdose and death in pregnancy and postpartum period – national conversations and why they matter

Indiana Perinatal Substance Use Conference

HEALTH
UNIVERSITY OF UTAH

Marcela Smid
Maternal Fetal Medicine
Addiction Medicine



DISCLOSURE

- Medical advisory committee for Gilead Science Inc. for hepatitis C treatment for pregnant and postpartum women
- Funded by the NIH K12 Women's Reproductive Health Research grant 2018-2020

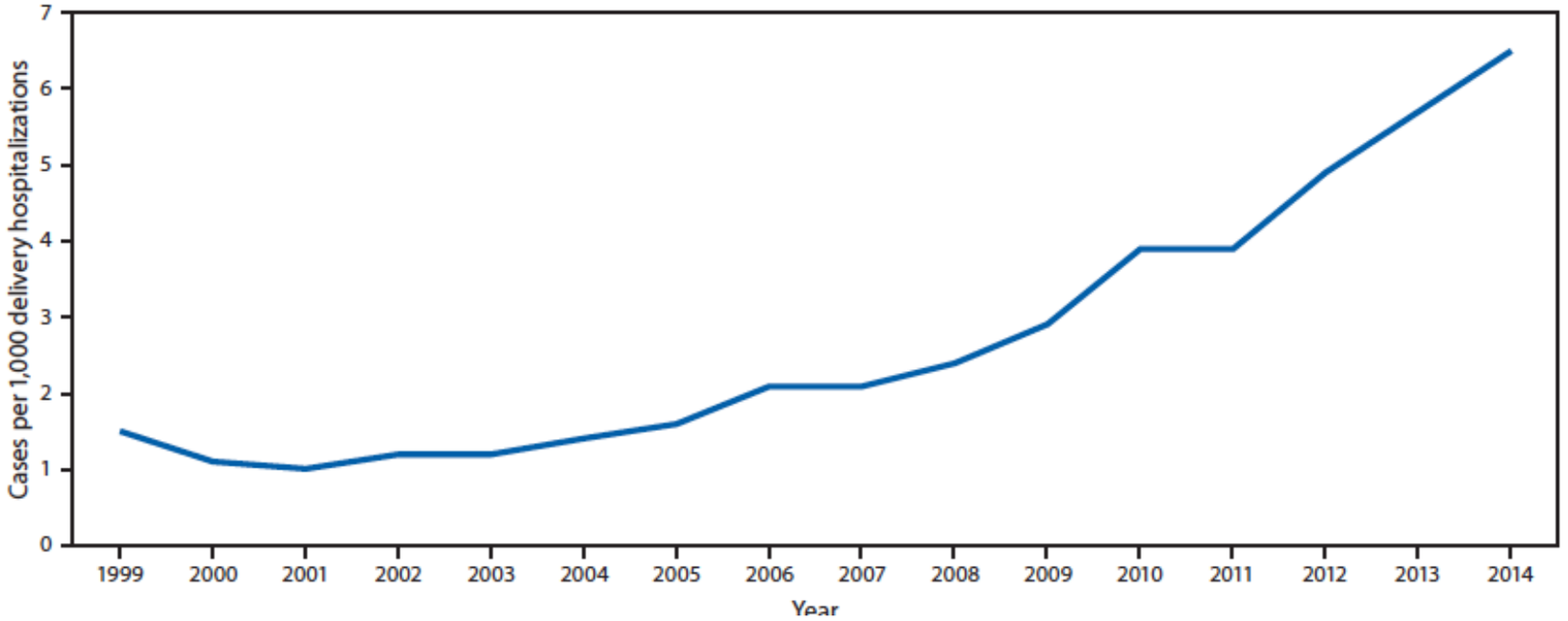
OBJECTIVES

- Understand current data sources on drug-related and suicides death among pregnant and postpartum individuals
- Review national discussions among maternal mortality review committees' determination of pregnancy related versus pregnancy associated drug-related deaths and suicides
- Discuss methods of determining perinatal substance use through anonymous cord prevalence testing

PREGNANCY AND OPIOID USE DISORDER

- Rates of pregnancy complicated by opioid use disorder **quadrupled** 1999-2014 (Haight et al 2018)

FIGURE 1. National prevalence of opioid use disorder per 1,000 delivery hospitalizations* — National Inpatient Sample (NIS),† Healthcare Cost and Utilization Project (HCUP), United States, 1999–2014



Opioid Use Disorder Documented at Delivery Hospitalization — United States, 1999–2014

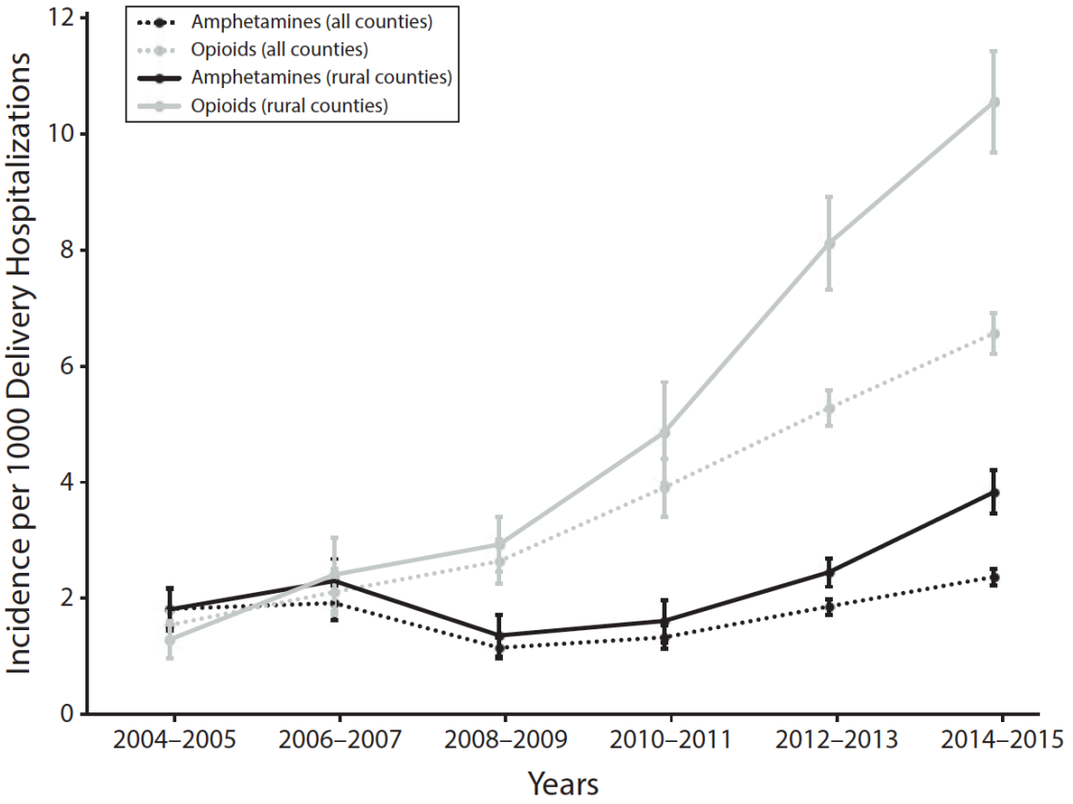
Sarah C. Haight, MPH[1,2]; Jean Y. Ko, PhD[1,3]; Van T. Tong, MPH[1]; Michele K. Bohm, MPH[4]; William M. Callaghan, MD[1]

PREGNANCY AND METHAMPHETAMINE

Amphetamine- and Opioid-Affected Births: Incidence, Outcomes, and Costs, United States, 2004–2015

Lindsay K. Admon, MD, MSc, Gavin Bart, MD, PhD, Katy B. Kozhimannil, PhD, MPA, Caroline R. Richardson, MD, Vanessa K. Dalton, MD, MPH, and Tyler N. A. Winkelman, MD, MSc

- 0.2% of deliveries between 2004-2015 were affected by amphetamine use
- Rural counties
  - **1% deliveries in rural West** complicated by amphetamines use
  - **5.2% in highest use areas**

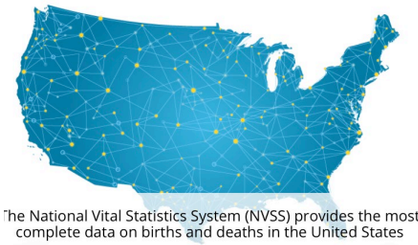


Note. The sample size was n = 47 164 263. All data are survey-weighted and represented as rate per 1000 delivery hospitalizations. Whiskers indicate 95% confidence intervals.

FIGURE 1—National Trends in Amphetamine and Opioid Use Among Delivering Women: National Inpatient Sample, United States, 2004–2015

SOURCES OF DATA FOR MATERNAL DEATH

- National Vital Statistics Systems



The National Vital Statistics System (NVSS) provides the most complete data on births and deaths in the United States

- Pregnancy Mortality Surveillance System

-
- Maternal Mortality Review Committees

DEFINITIONS

Pregnancy-Associated Death

A death during or within one year of pregnancy, regardless of the cause. These deaths make up the universe of maternal mortality; within that universe are pregnancy-related deaths and pregnancy-associated, but not related deaths.

Pregnancy-Related Death

A death during or within one year of pregnancy, from a pregnancy complication, a chain of events initiated by pregnancy, or the aggravation of an unrelated condition by the physiologic effects of pregnancy.

Pregnancy-Associated, but Not Related Death

A death during or within one year of pregnancy, from a cause that is not related to pregnancy.

Pregnancy-Related Mortality Ratio

The number of pregnancy-related deaths (using the above definition) per 100,000 live births.

Preventability

A death is considered preventable if there was at least some chance of the death being prevented by one or more reasonable changes to patient, family, provider, facility, system, and/or community factors. This definition is used by MMRCs to determine if a death they review is preventable.

Maternal Death

The death of a woman while pregnant or within 42 days of termination of pregnancy, regardless of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental causes. This definition is used by the National Center for Health Statistics and the World Health Organization.

Maternal Mortality Ratio

The number of maternal deaths (using the above definition) per 100,000 live births. The maternal mortality ratio is also colloquially called the maternal mortality rate.

Maternal Mortality

This site uses the term maternal mortality to encompass the topic of deaths during pregnancy, childbirth, and the postpartum period up to 365 days from the end of pregnancy.

https://reviewtoaction.org/learn/definitions

POSTPARTUM DEATHS

- California hospital and death data
- 300 postpartum women (up to one year) died between 2010-2012
- Drug-related and suicides nearly 1:5 deaths
  - 74% had at least one emergency room or hospital visit between delivery and death

TABLE 2
Causes and associated 12 month incidence rates of postpartum death, ranked in descending order, among women delivering in California, 2010–2012

Underlying cause	Deaths, n	Incidence rate (per 100,000 person-years)	95% CI around incidence rate
Obstetric complications/disease	69	6.52	5.15–8.25
Drug related	39	3.68	2.69–5.04
Circulatory system disease	36	3.40	2.45–4.71
Cancer	34	3.21	2.29–4.49
Other unintentional injuries	33	3.12	2.22–4.38
Homicide	17	1.61	1.00–2.58
Suicide	15	1.42	0.85–2.35
All other causes	57	5.38	4.15–6.98

Goldman-Mellor and Margerison. Drug-related and suicide death as causes of postpartum maternal death. Am J Obstet Gynecol 2019.

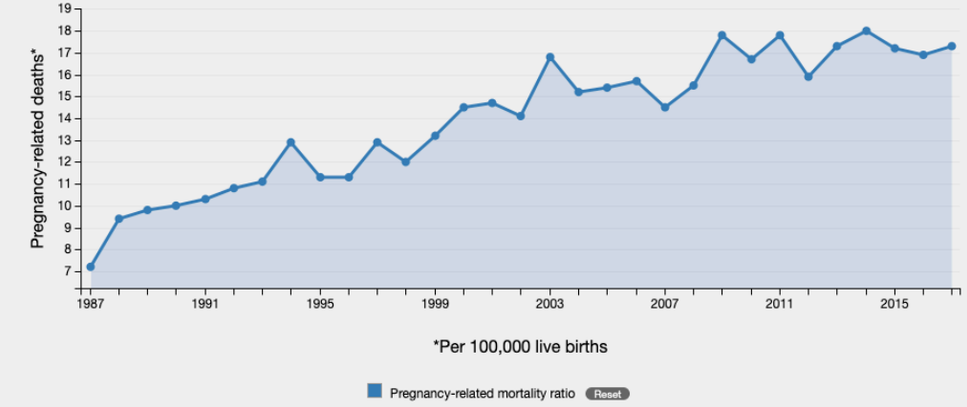
OBSTETRICS

Maternal drug-related death and suicide are leading causes of postpartum death in California

Sidra Goldman-Mellor, PhD; Claire E. Margerison, PhD

MATERNAL DEATHS

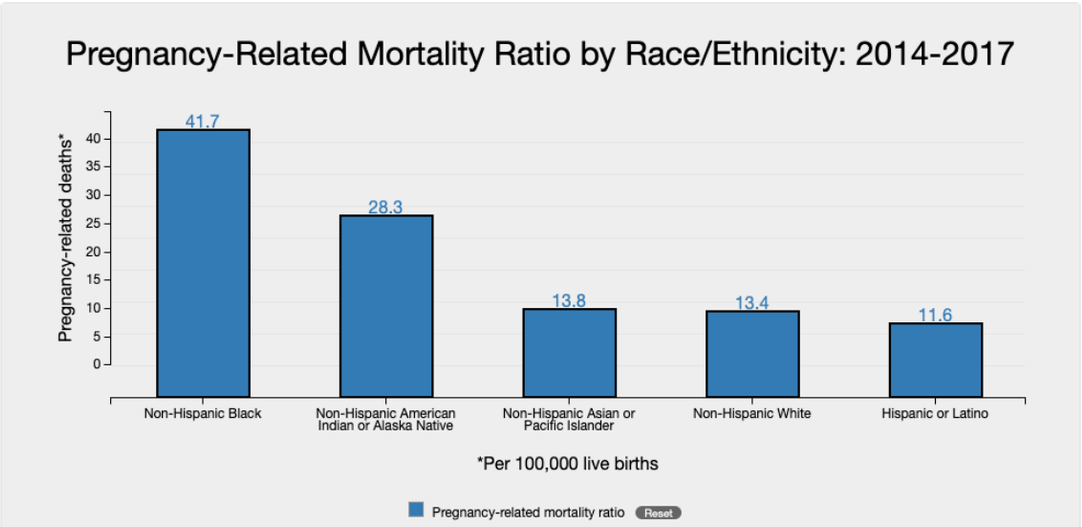
Trends in Pregnancy-Related Deaths



Data Table

	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	199
Pregnancy-related mortality ratio	7.2	9.4	9.8	10	10.3	10.8	11.1	12.9	11.3	11.3	12.9	

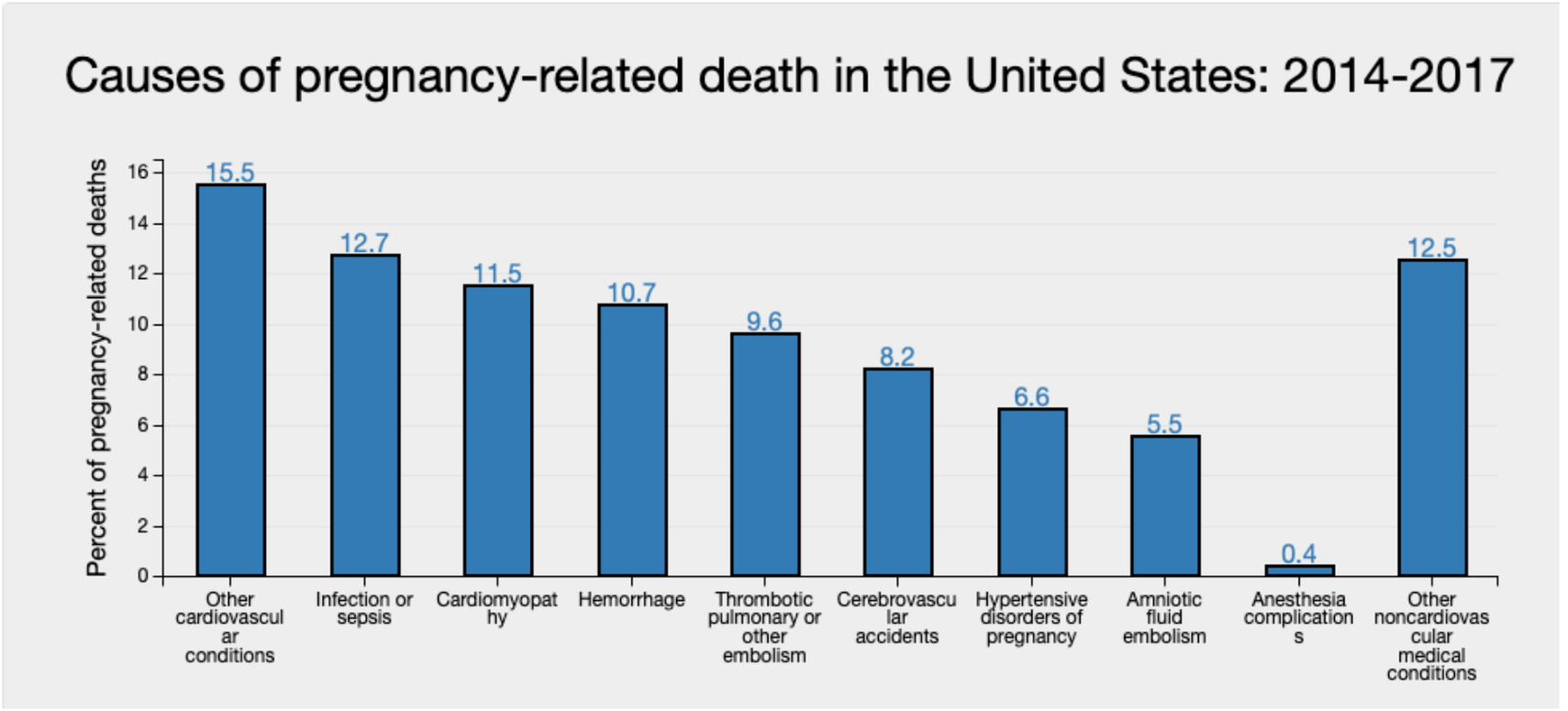
Pregnancy-Related Deaths by Race/Ethnicity



Data Table

	Non-Hispanic Black	Non-Hispanic American Indian or Alaska Native	Non-Hispanic Asian or Pacific Islander	Non-Hispan
Pregnancy-related mortality ratio	41.7	28.3	13.8	

MATERNAL DEATHS



POSTPARTUM DEATHS

nization [WHO]/ICD-10 definition).[10] Given the limited data available for each case, we cannot ascertain whether injury deaths such as drug overdoses, suicides or homicides, or cancer-related deaths during pregnancy or within 1 year postpartum are pregnancy related, and therefore, we consider such deaths pregnancy associated. In countries where more

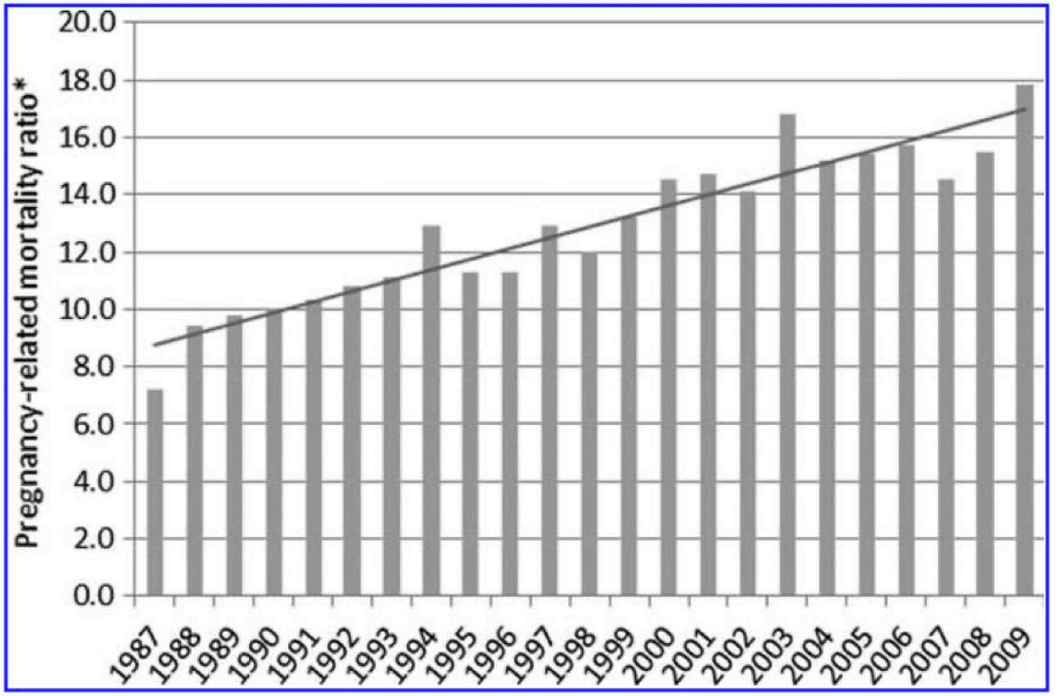


FIG. 1. Trends in pregnancy-related mortality in the United States, 1987–2009. *Number of pregnancy-related deaths per 100,000 live births per year; test for trend $p < 0.001$. Data from Centers for Disease Control and Prevention.[2]

Maternal Mortality and Morbidity in the United States: Where Are We Now?

Andreea A. Creanga, MD, PhD, Cynthia J. Berg, MD, MPH, Jean Y. Ko, PhD, Sherry L. Farr, PhD, Van T. Tong, MPH, F. Carol Bruce, RN, MPH, and William M. Callaghan, MD, MPH

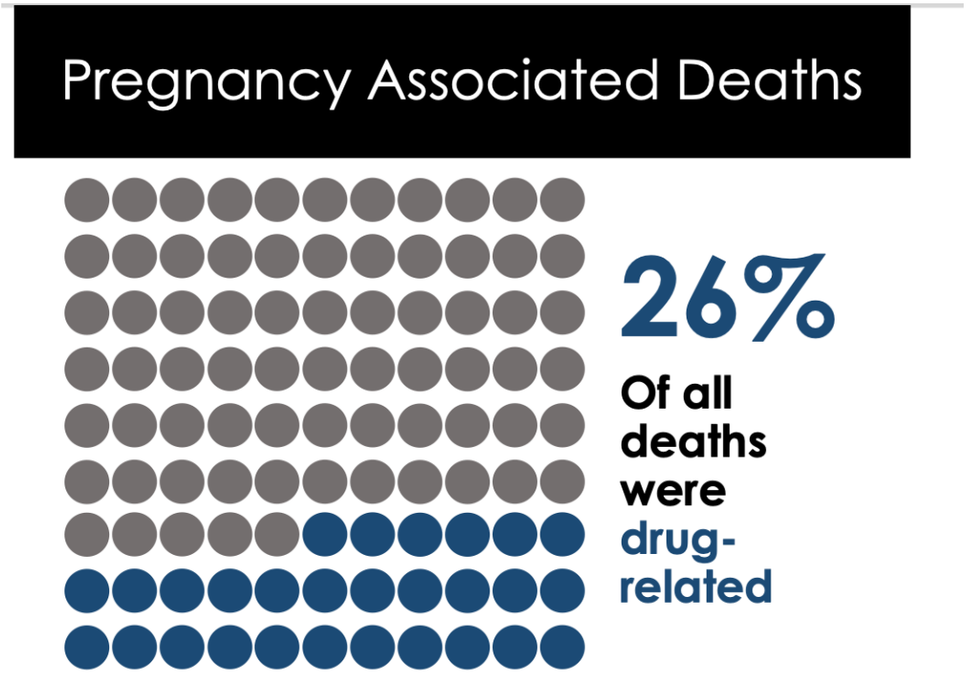
PREGNANCY AND DRUG INDUCED DEATHS

Maternal Morbidity and Mortality: *Original Research*

Pregnancy-Associated Death in Utah

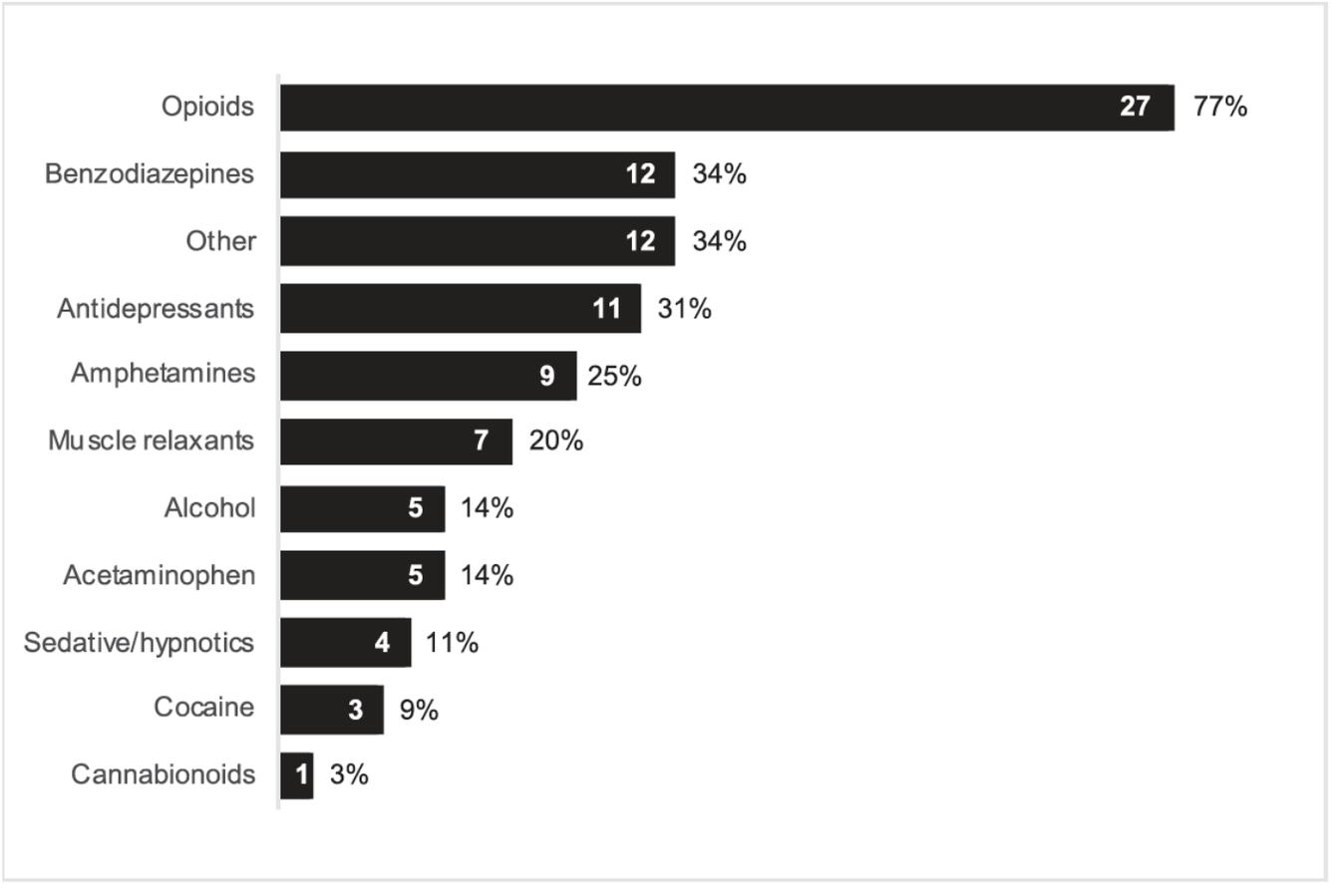
Contribution of Drug-Induced Deaths

Marcela C. Smid, MD, Nicole M. Stone, MPH, Laurie Baksh, MPH, Michelle P. Debbink, MD, PhD, Brett D. Einerson, MD, Michael W. Varner, MD, Adam J. Gordon, MD, and Erin A. S. Clark, MD



PREGNANCY AND DRUG INDUCED DEATHS

- Polysubstance use 83%
- 66% had 3 or more substances



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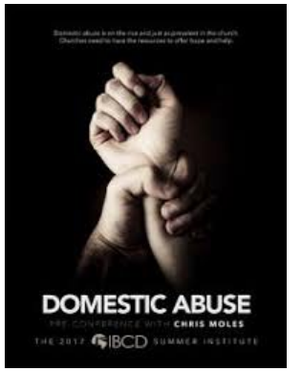
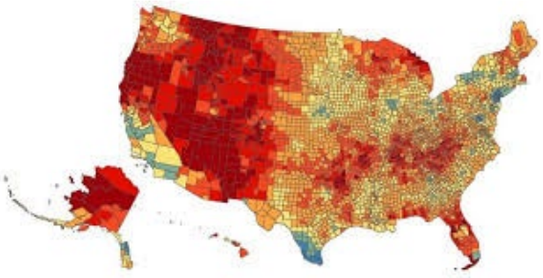
PREGNANCY AND DRUG RELATED DEATHS

Characteristic	Total (n=35)
Age (y)	
15–19	2 (5.7)
20–34	28 (80.0)
35 or more	5 (14.3)
Married	17 (48.6)
Medicaid at delivery	16 (45.7)
Drug misuse or substance use disorder	19 (54.2)
Chronic pain	15 (42.9)
Obesity	13 (37.1)
Mental health diagnosis	27 (77.1)
Depression	24 (69)
Anxiety	19 (54.2)
Schizophrenia	1 (2.9)
Bipolar	2 (5.7)
Prior suicide attempt	8 (22.9)
Prior overdose	9 (25.7)
Prior mental health hospitalization	6 (17.1)
History of lifetime abuse (emotional, mental, physical, sexual)	9 (25.7)
Intimate partner violence	6 (17.1)
Mental health services documented	9 (25.7)
Social work referral documented	14 (40.0)
Prenatal care record	n=26
Drug-related concern in prenatal chart	21 (60.0)
Delivery care record	n=24
Drug-related concern in delivery record (n=24)	18 (75.0)
No. of infants	31
Department of Child and Family Services involvement	7 (22.5)





PREGNANCY AND DRUG RELATED DEATHS

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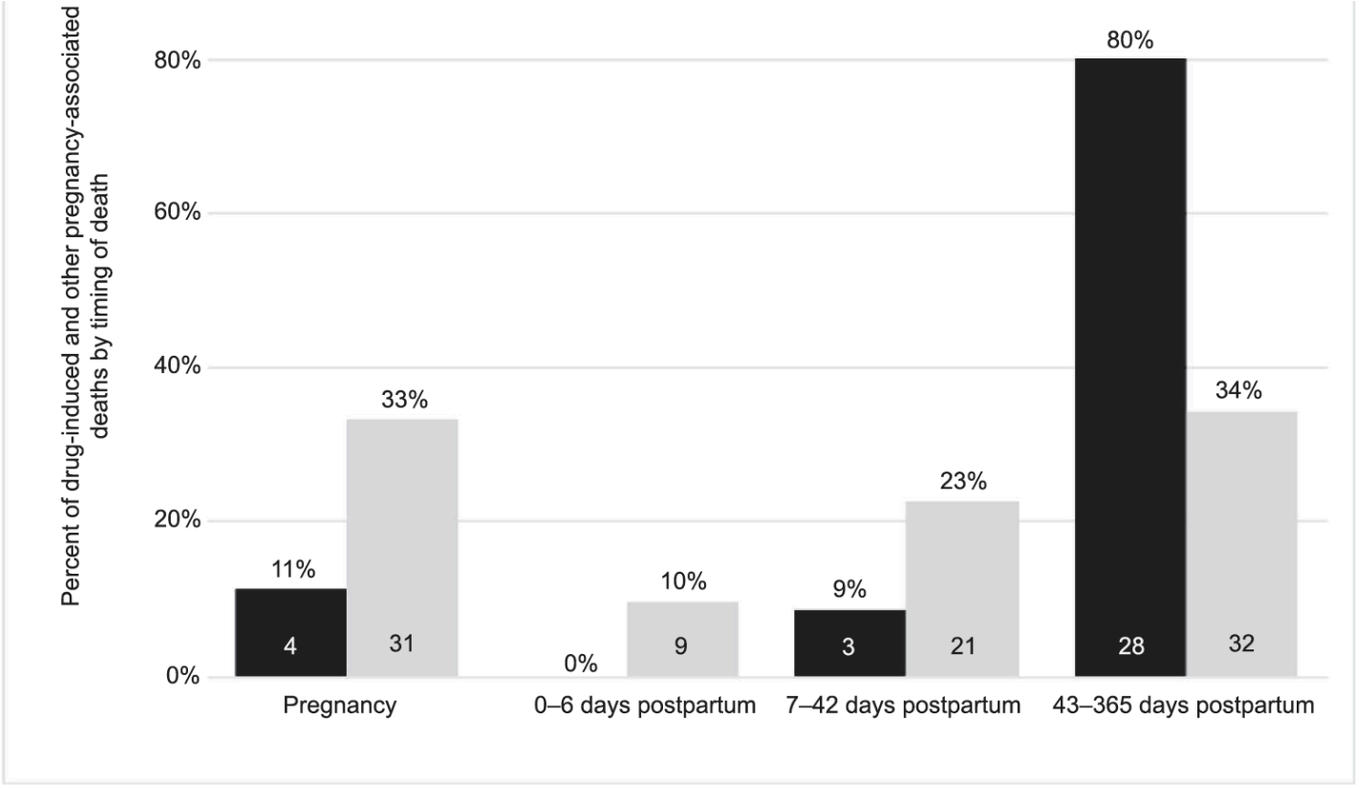
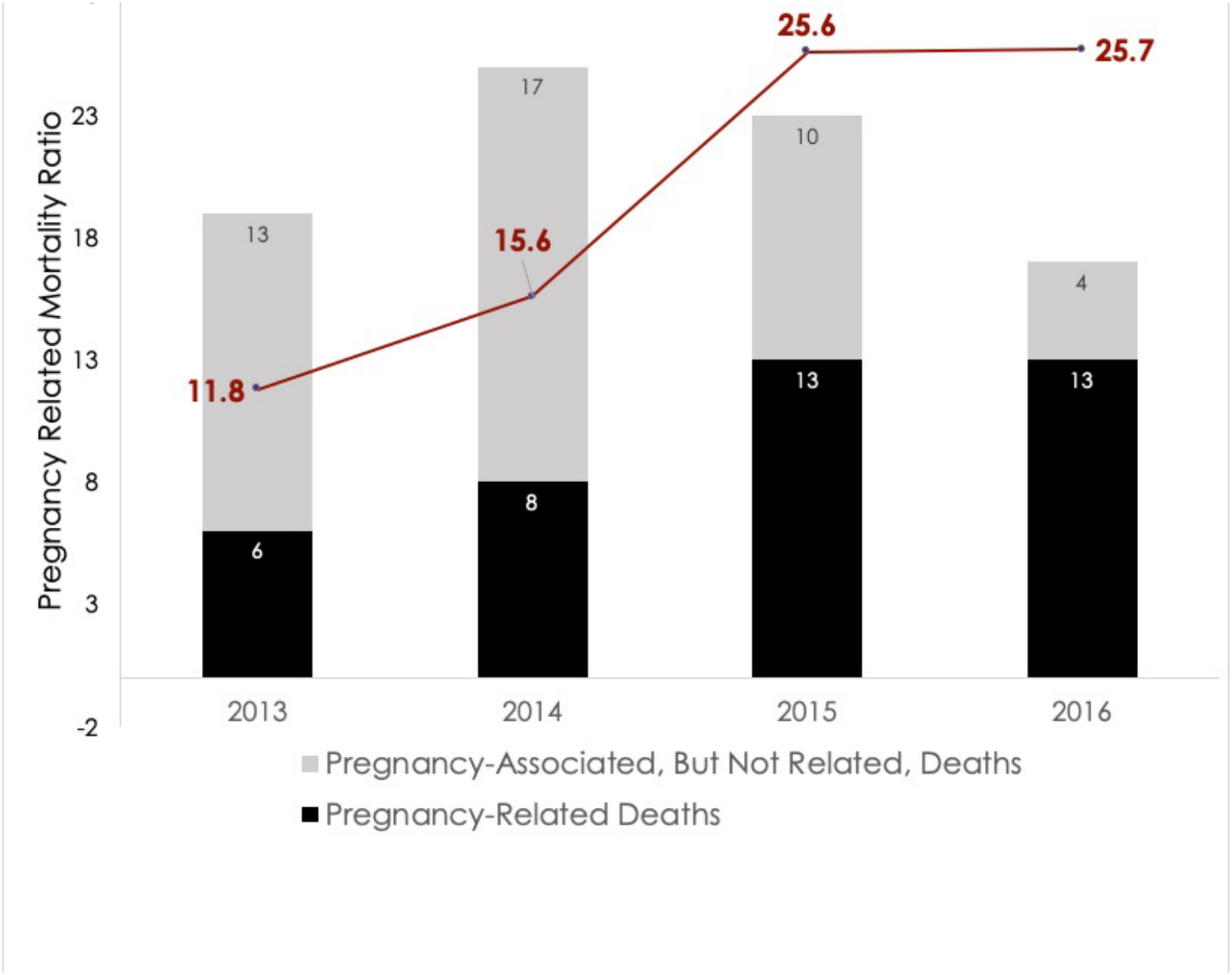


Fig. 1. Proportion of pregnancy-associated, drug-induced deaths vs all pregnancy-associated deaths 2005–2014 (N=136).
Smid. Pregnancy-Associated Drug-Induced Deaths in Utah. Obstet Gynecol 2019.

WHAT HAPPENED IN UTAH IN 2015?



PREGNANCY RELATED VERSUS ASSOCIATED

Original Research

Standardized Criteria for Review of Perinatal Suicides and Accidental Drug-Related Deaths

Marcela C. Smid, MD, MS, Jewel Maeda, CNM, MPH, Nicole M. Stone, MPH, Heidi Sylvester, CPM, Laurie Baksh, MPH, Michelle P. Debbink, MD, PhD, Michael W. Varner, MD, and Torri D. Metz, MD, MS

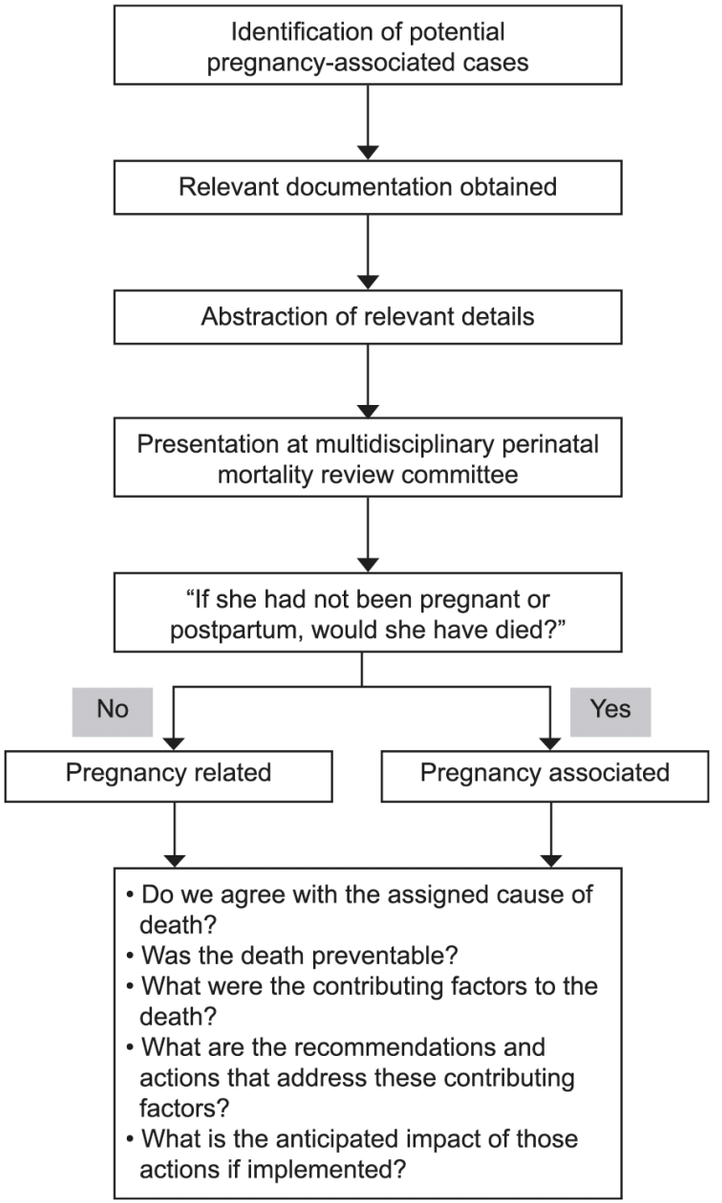


Fig. 1. Flow diagram of Utah's Perinatal Mortality Review Committee process.

PREGNANCY RELATED CRITERIA

Table 1. Standardized Criteria Applied to Accidental Drug-Related Deaths and Suicides

Standardized Criteria for Accidental Drug-Related Deaths and Suicides	Case Examples	No. of Times Identified in Accidental Drug-Related Death	No. of Times Identified in Suicide
1. Pregnancy complication		**7**	**1**
a. Increased pain directly attributable to pregnancy or postpartum events leading to self-harm or drug use that is implicated in suicide or accidental death	Back pain, pelvic pain, kidney stones, cesarean incision, or perineal tear pain	0	0
b. Traumatic event in pregnancy or postpartum with a temporal relationship between the event leading to self-harm or increased drug use and subsequent death	Stillbirth, preterm delivery, diagnosis of fetal anomaly, traumatic delivery experience, relationship destabilization due to pregnancy, removal of child(ren) from custody	7	1
c. Pregnancy-related complication likely exacerbated by drug use leading to subsequent death	Placental abruption or preeclampsia in setting of drug use	0	0

PREGNANCY RELATED DEATH

Table 1. Standardized Criteria Applied to Accidental Drug-Related Deaths and Suicides

Standardized Criteria for Accidental Drug-Related Deaths and Suicides	Case Examples	No. of Times Identified in Accidental Drug-Related Death	No. of Times Identified in Suicide
2. Chain of events initiated by pregnancy		**9**	**3**
a. Cessation or attempted taper of medications for pregnancy-related concerns (neonatal or fetal risk or fear of Child Protective Service involvement) leading to maternal destabilization or drug use and subsequent death	Substance use pharmacotherapy (methadone or buprenorphine), psychiatric medications, pain medications	3	1
b. Inability to access inpatient or outpatient drug or mental health treatment due to pregnancy	Health care professionals uncomfortable with treating pregnant women, facilities not available that accept pregnant women	0	0
c. Perinatal depression, anxiety, or psychosis resulting in maternal destabilization or drug use and subsequent death	Depression diagnosed in pregnancy or postpartum resulting in suicide	1	2
d. Recovery or stabilization of substance use disorder achieved during pregnancy or postpartum with clear statement in records that pregnancy was motivating factor with subsequent relapse and subsequent death	Relapse leading to overdose due to decreased tolerance or polysubstance use	5	0

Drug-Related Deaths

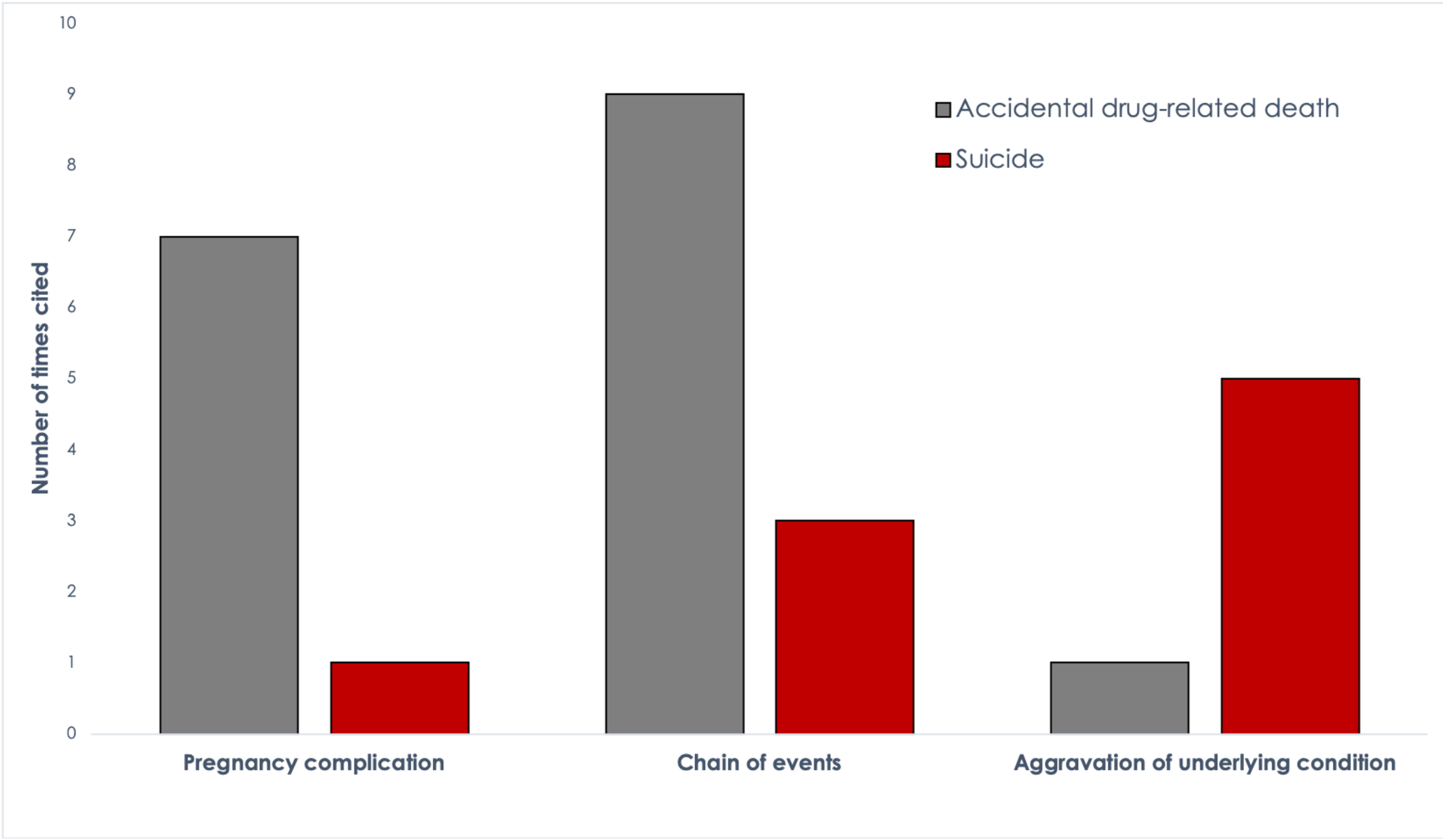
Marcela C. Smid, MD, MS, Jewel Maeda, CNM, MPH, Nicole M. Stone, MPH, Heidi Sylvester, CPM, Laurie Baksh, MPH, Michelle P. Debbink, MD, PhD, Michael W. Varner, MD, and Torri D. Metz, MD, MS

PREGNANCY RELATED VERSUS ASSOCIATED

Table 1. Standardized Criteria Applied to Accidental Drug-Related Deaths and Suicides

Standardized Criteria for Accidental Drug-Related Deaths and Suicides	Case Examples	No. of Times Identified in Accidental Drug-Related Death	No. of Times Identified in Suicide
subsequent death			
3. Aggravation of underlying condition by pregnancy		**1**	**5**
a. Worsening of underlying depression, anxiety, or other psychiatric condition in pregnancy or the postpartum period with documentation that mental illness led to drug use or self-harm and subsequent death	Pre-existing depression exacerbated in the postpartum period leading to suicide	1	5
b. Exacerbation, undertreatment, or delayed treatment of pre-existing condition in pregnancy or postpartum leading to use of prescribed or illicit drugs resulting in death, or suicide	Undertreatment of chronic pain leading to misuse of medications or use of illicit drugs, resulting in death	0	0
c. Medical conditions secondary to drug use in setting of pregnancy or postpartum that may be attributable to pregnancy-related physiology and increased risk of complications leading to death	Stroke or cardiovascular arrest due to stimulant use	0	0

PREGNANCY RELATED DEATHS



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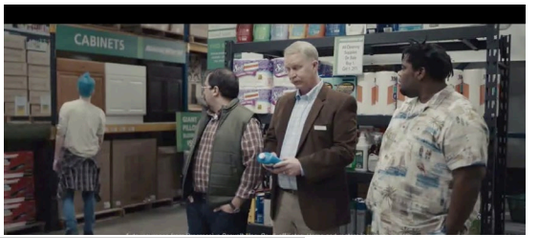

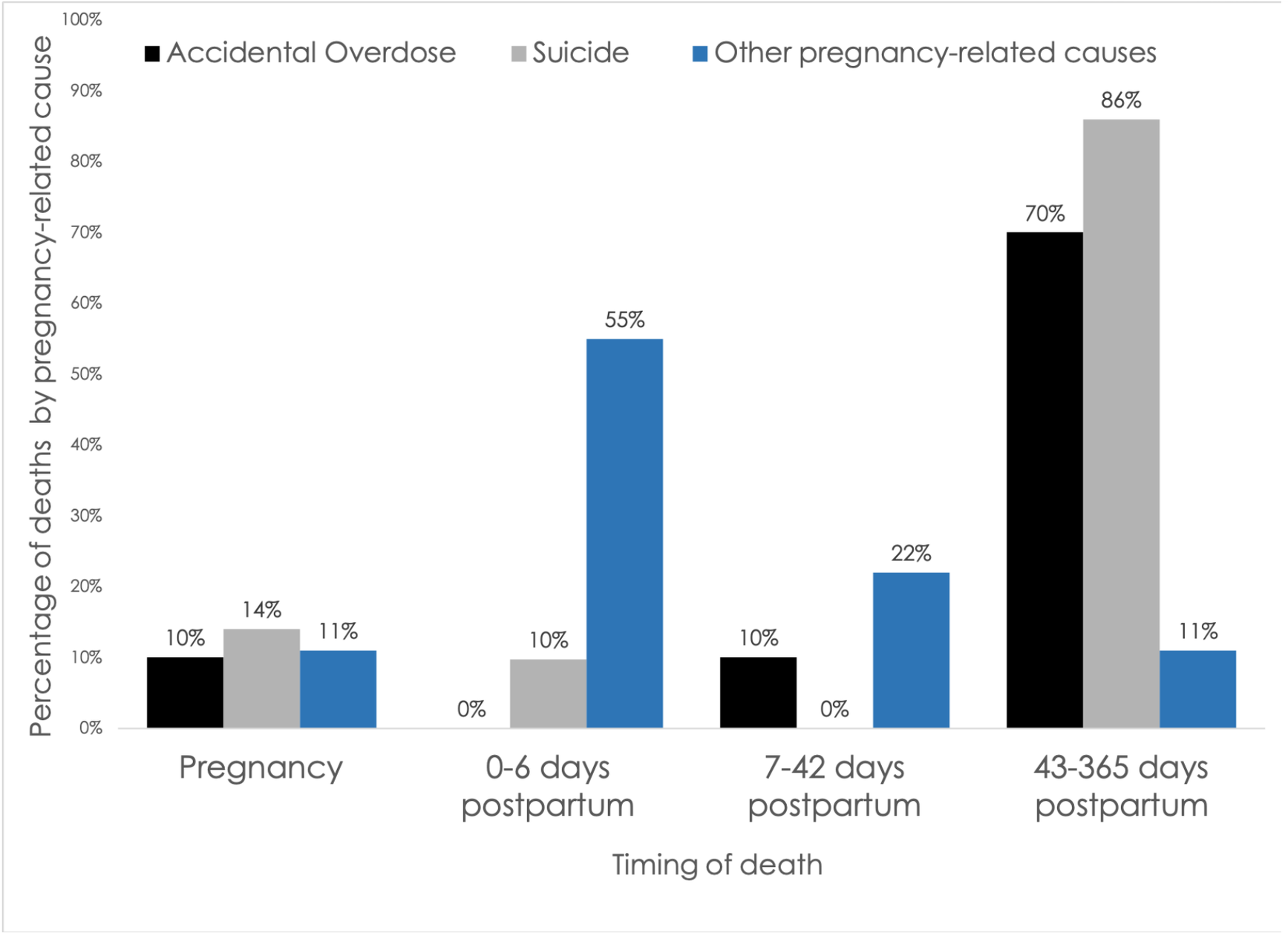

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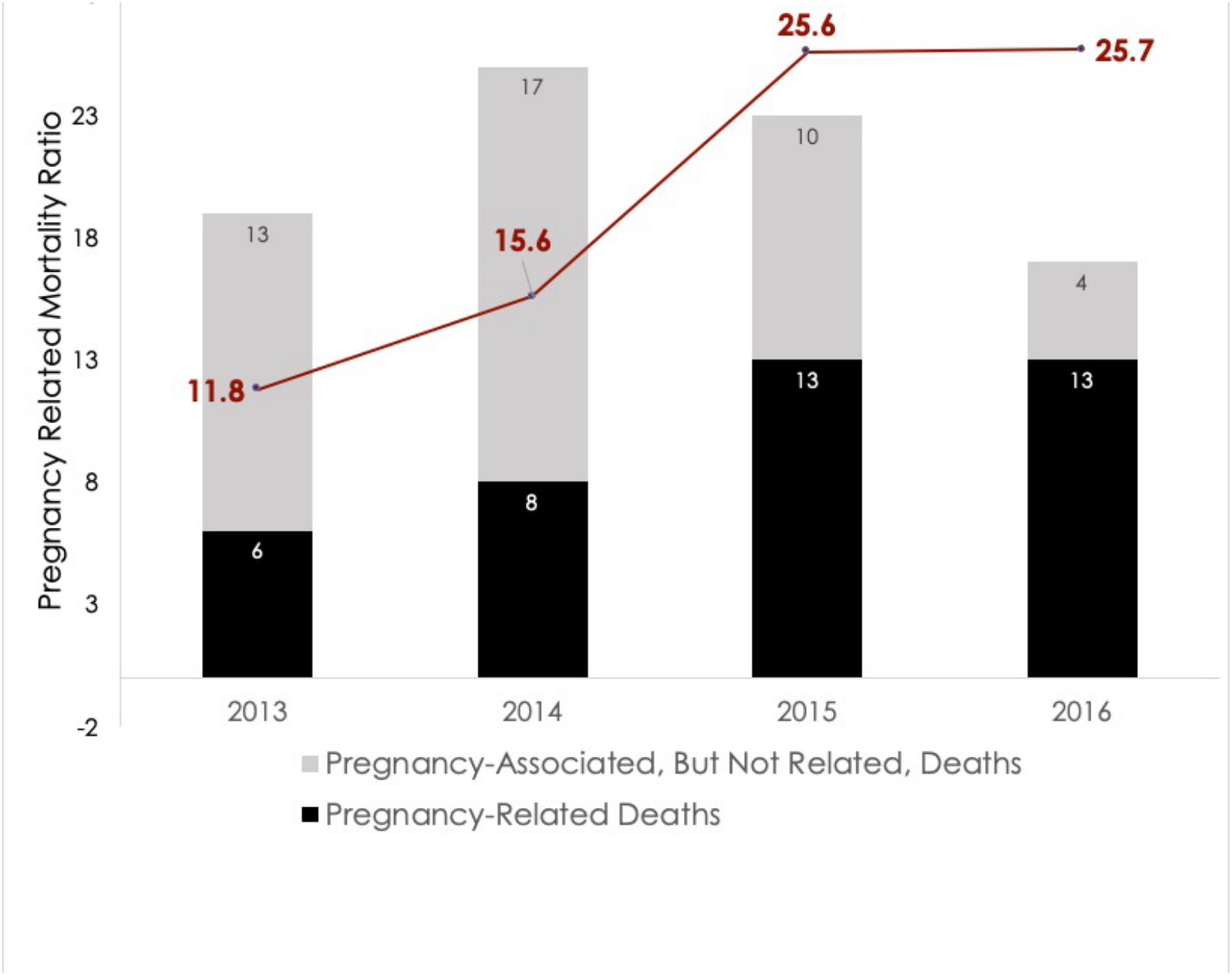

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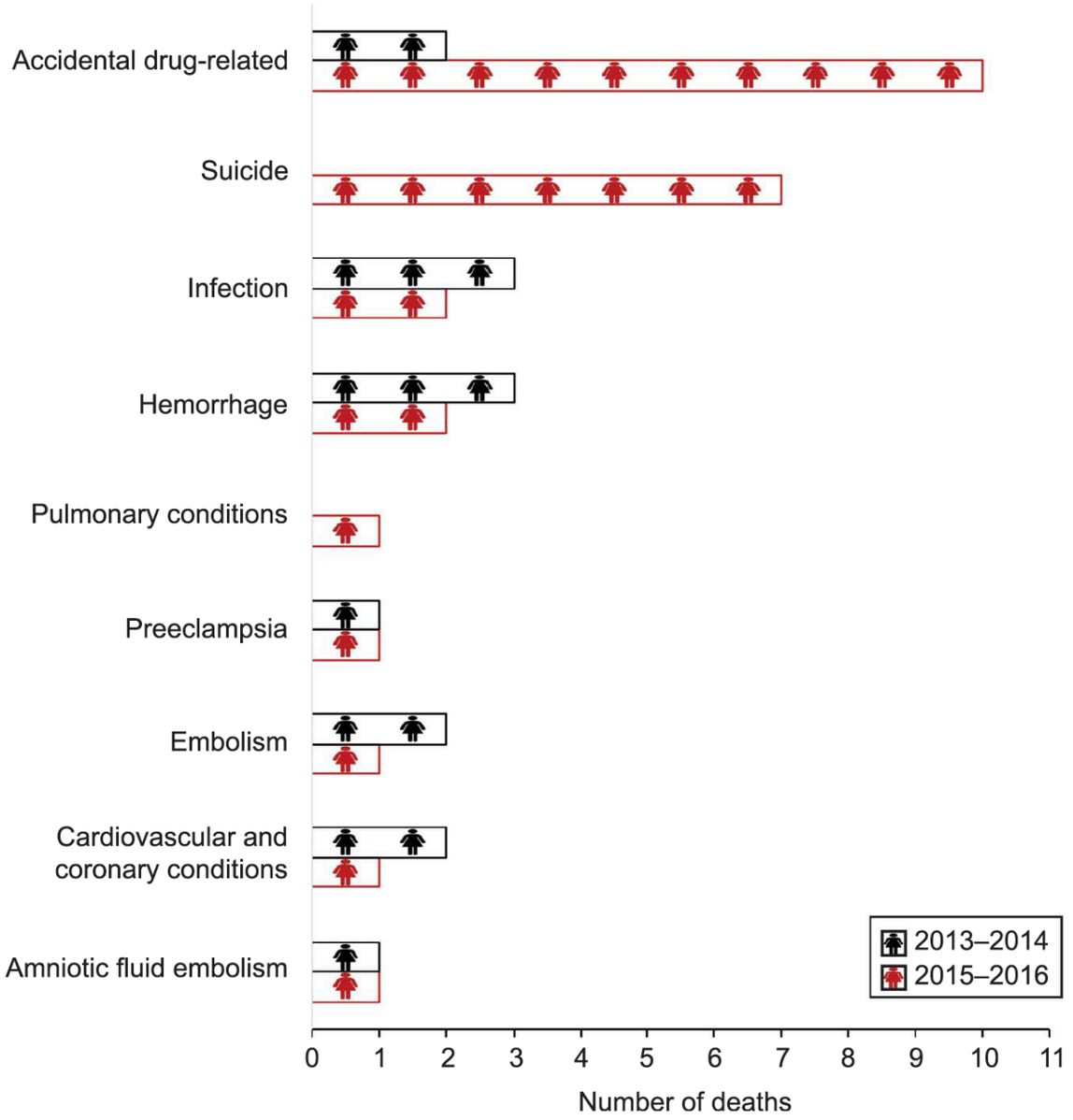
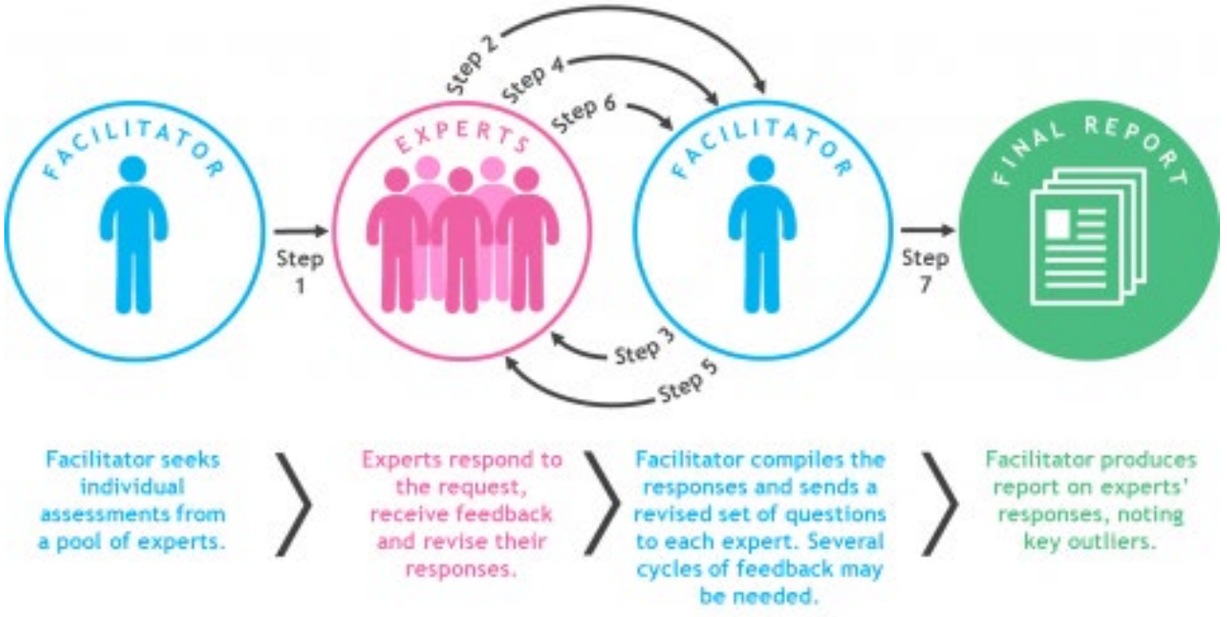


Fig. 2. Causes of pregnancy-related deaths, 2013–2014 and 2015–2016.

Smid. Drug-Related Death and Suicide Classification Criteria. Obstet Gynecol 2020.

DELPHI METHOD. FOR PREGNANCY RELATED CRITERIA

- National consensus
- Representative from each state and other experts (over 50 participants)
- Currently in Round 2



RECOMMENDATIONS FROM MMRC

- Universal screening
- Prevalence estimates 4-40%
  - Population
  - Substances
  - "Risk-based" versus universal screening
  - Trimester of screening

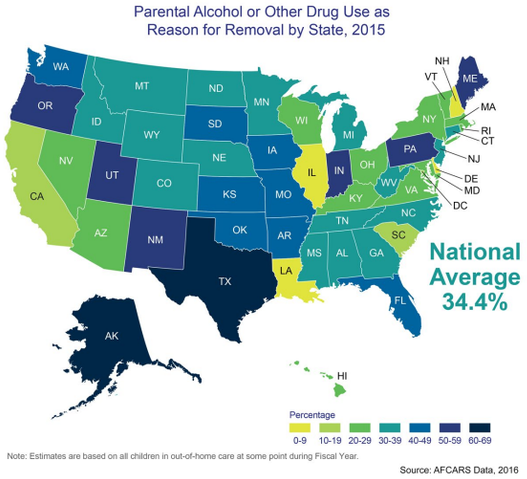
Quick Screen **Question:** **<u>In the past year</u>, how often have you used the following?**	**Never**	**Once or Twice**	**Monthly**	**Weekly**	**Daily or Almost Daily**
Alcohol • **For men, 5 or more drinks a day** • **For women, 4 or more drinks a day**					
Tobacco Products					
Prescription Drugs for Non-Medical Reasons					
Illegal Drugs					

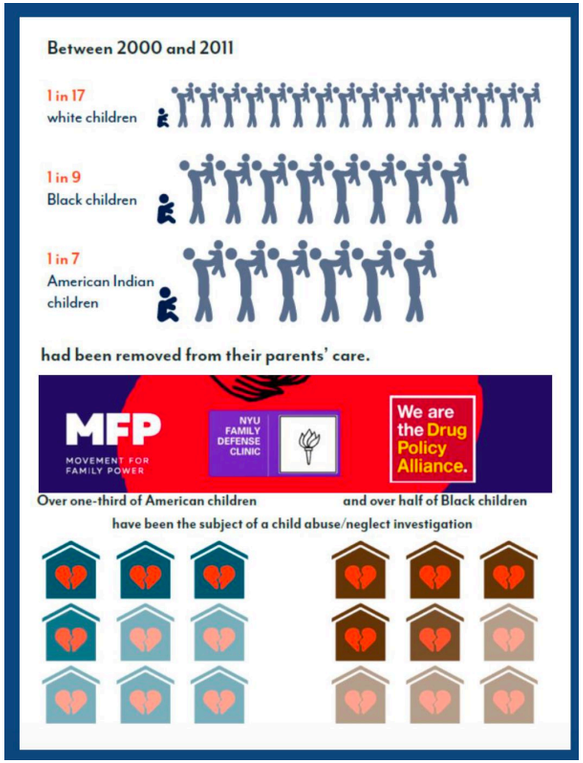
BACKGROUND

- Prevalence based on biological sampling up to ten fold higher than **self-report**

- Stigma and legal implications of disclosure

- **Reliable population-based prevalence difficult to obtain**





PRIOR PREVALENCE UTAH STUDIES

The Prevalence of Prenatal Opioid and Other Drug Use in Utah

Karen F. Buchi, MD [1] Carla Suarez, BS [1] Michael W. Varner, MD [2]

- March-June 2010
- 13 labor and delivery units
- 850 cord samples
- 6.8% pos; 4.7% opioids

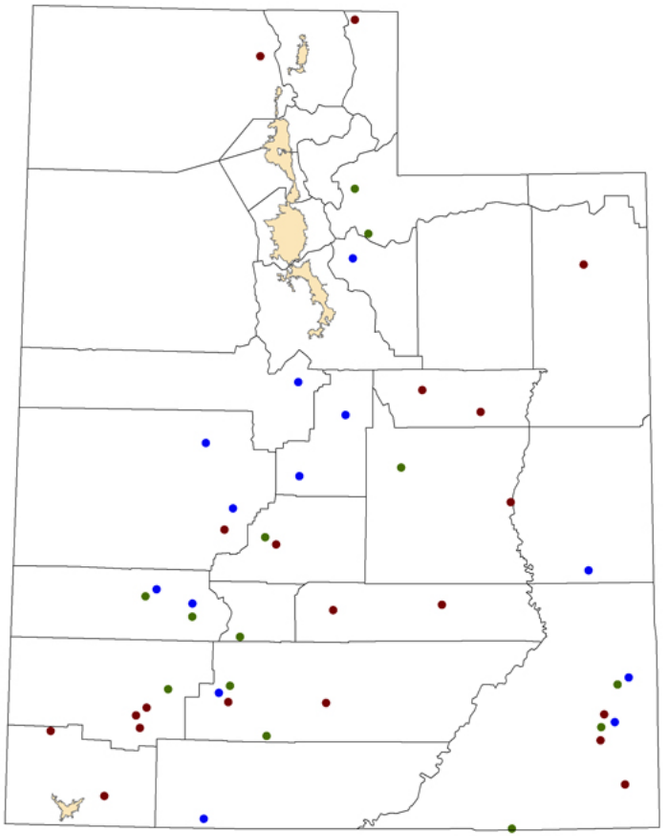
Positive umbilical cord drug screen	58 (6.8%)
Alcohol	3 (0.4%)
Methamphetamine	1 (0.1%)
Barbiturates	6 (0.7%)
Benzodiazepines	5 (0.6%)
Cocaine	1 (0.1%)
Marijuana	4 (0.4%)
Opiates/opioids	40 (4.7%)
Hydrocodone	10 (1.2%)
Morphine	15 (1.2%)
Methadone	2 (0.2%)
Meperidine	10 (1.2%)
Tramadol	2 (0.2%)
Oxycodone	6 (0.7%)

Table 2 Comparison of Maternal and Infant Characteristics between Opioid-Positive and Opioid-Negative Cord Samples

	Opioid-Positive Cord Samples ($n = 40$)	Opioid-Negative Cord Samples ($n = 810$)	p Value
Unmarried (%)	45	19	<0.01
Medicaid/no insurance (%)	56	32	<0.01
Tobacco use during this pregnancy (%)	33	4	<0.0001
Mean birth weight, g (SD)	2970 (671)	3277 (502)	<0.0002
Mean gestational age, wk (SD)	37.5 (2.6)	38.5 (1.6)	<0.001

METHODS

- **Population-based** cross-sectional study
  - All Utah Labor and Delivery units (n=45) invited
- **Target number** of umbilical cords calculated for each hospital based on 2017 delivery volume
  - Oversampled of **rural and frontier** hospitals
  - Sampling weights to account for sampling strategy, and post stratification weight to adjust for non-response within region



METHODS

- **Consecutive deliveries** at each hospital until target number reached
  - No inclusion or exclusion criteria
  - No patient identifying information collected
  - Basic non-identifiable demographics from medical record

UMBILICAL CORD PREVALENCE STUDY – Sample Collection Half Sheet

all information on this form is to be taken from medical records. Please do not directly ask the patient

<table>
<tr>
<td>Mother's Age (years)
☐ <19
☐ 20-34
☐ ≥ 35
☐ Unavailable/ unsure</td>
<td>Gestational Age at delivery (weeks.days)
☐ < 28w0d
☐ 28w0d – 31w6d
☐ 32w0d – 33w6d
☐ 34w0d – 36w6d
☐ 37w0d – 40w6d
☐ ≥41w0d
☐ Unknown/unsure

Mode of Delivery
☐ Vaginal
☐ Assisted vaginal (Forceps/Vacuum)
☐ Caesarean Section
☐ Unknown/unsure</td>
<td>Race
☐ American Indian/Alaska Native
☐ Asian
☐ Black/African American
☐ Native Hawaiian/Other Pacific Islander
☐ White/Caucasian
☐ Unavailable/Unknown

Ethnicity
☐ Hispanic/Latino
☐ Not Hispanic/Latino
☐ Unknown/unsure</td>
<td rowspan="2">Medications/Substance Use During Pregnancy
☐ Tobacco
☐ Vaping
☐ Alcohol
☐ Prescription opioids
☐ Prescription benzodiazepines
☐ Prescription stimulant (Adderall ®, Ritalin ®, Concerta ®)
☐ Gabapentin
☐ Anti-depressant
☐ Anti-seizure medication
☐ Sleeping aids
☐ Marijuana
☐ Opioids (heroin)
☐ Methamphetamine
☐ Cocaine
☐ Other
☐ None
Specify:_____

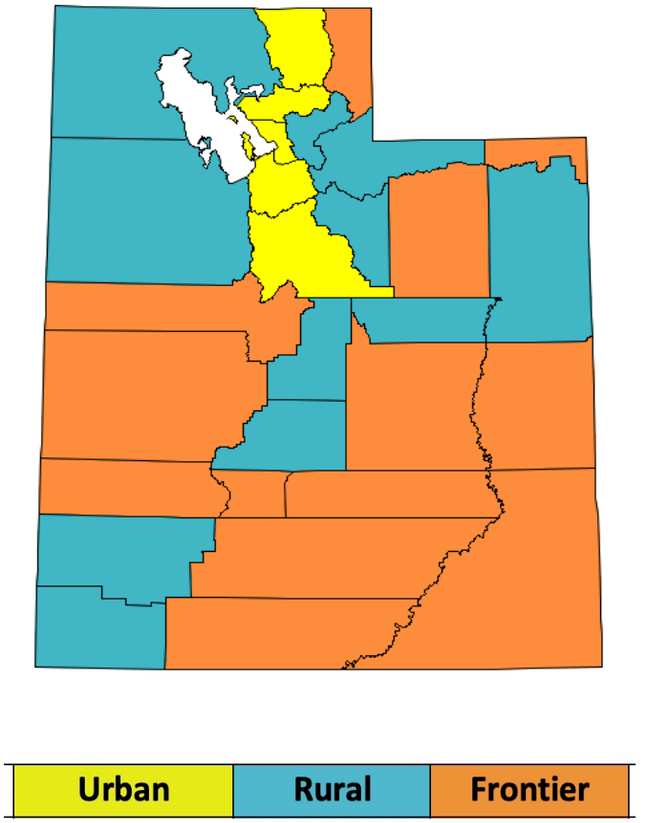
☐ Unknown/unsure</td>
</tr>
<tr>
<td>Marital Status
☐ Single
☐ Married
☐ Unavailable/ unsure</td>
<td>Insurance Status
☐ Commercial
☐ Medicaid/Medicare
☐ Uninsured
☐ Military
☐ Unknown/unsure</td>
<td>Medical Hx
☐ Diabetes (pregestational or gestational)
☐ Chronic hypertension
☐ Pre-eclampsia/ eclampsia
☐ Obesity (BMI ≥ 30)
☐ Hepatitis C
☐ Other
Specify:_____
☐ Unavailable/unknown</td>
</tr>
<tr>
<td>Birth Weight
☐ <2500 g
☐ ≥ 2500 g
☐ Unknown/ unsure</td>
<td>1 Minute APGAR
☐ < 7
☐ ≥ 7
☐ Unknown/unsure</td>
<td>5 Minute APGAR
☐ < 7
☐ ≥ 7
☐ Unknown/unsure</td>
<td># of Prenatal Visits
☐ None
☐ Limited (initiated at ≥ 20 weeks)
☐ Usual (initiated at < 20 weeks)
☐ Unknown/unsure</td>
</tr>
</table>

METHODS

- 4-6 inch umbilical cord segment
- Qualitative liquid chromatography/tandem mass spectrometry umbilical cord assay (ARUP Lab)
- Cord panel: opioids, amphetamines, other (zolpidem, PCP, gabapentin, butalbital) cocaine, benzodiazepines, cannabis, and alcohol metabolites
- Reflects **2-4 months** prior to delivery
  - ~ third trimester in term pregnancy
  - Not typically reflective of L&D exposure

METHODS

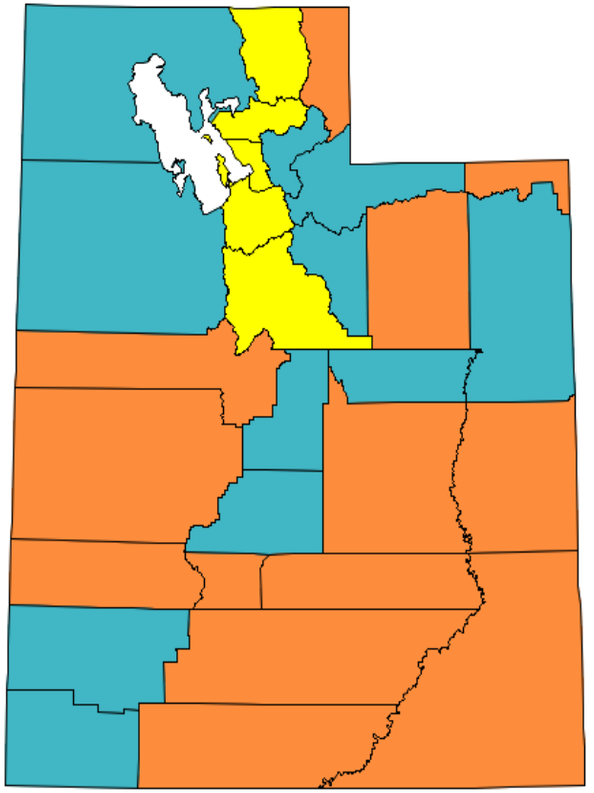
- Prevalence of prenatal cord positivity reported in weighted percentage
  - Overall
  - Region (urban, rural, frontier)
  - County



- Urban = population density > 100 people per square mile
- Rural = 6-99/sq mile
- Frontier is <6/ sq mile

RESULTS

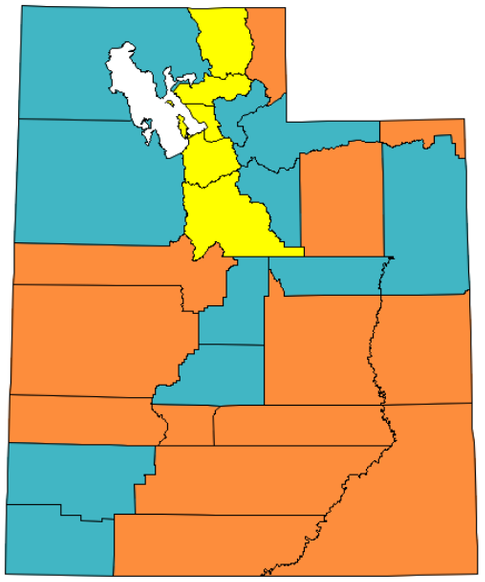
- **37 hospitals (82%)** participated
  - Nov 2019 – Nov 2020
- **1748 cord samples** analyzed
  - One cord insufficient sample
- Demographics
  - 76% White
  - 78% Married
  - 79% Age 20-34
  - 59% Commercial insurance (21% unknown)
- Obstetric characteristics
  - 91% started prenatal care < 20 weeks
  - 90% term delivery
  - 62% vaginal delivery
  - 3.5% tobacco use in pregnancy



RESULTS

- **Nearly 10%** of cords were positive for any substance

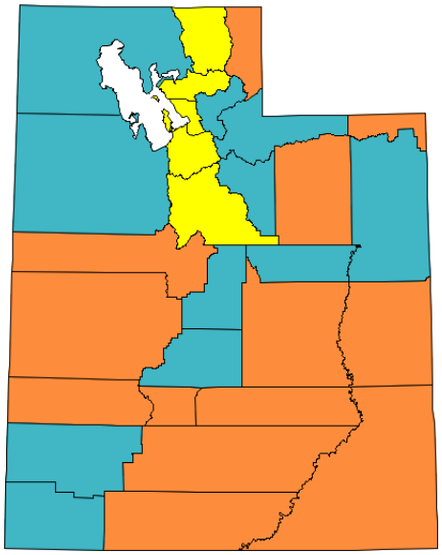
- **No difference** in urban, rural or frontier location



Substance		All	Urban	Rural	Frontier	p
	Unweighted N	**1748**	988	384	376	
	Weighted N	**1748**	1495	197	56	
Any Substance Use	In Cord	173 (9.9)	154 (10.3)	14 (7)	5 (9)	0.312
	In Cord or Medical Record	240 (13.7)	206 (13.8)	26 (13)	8 (14)	0.98

RESULTS

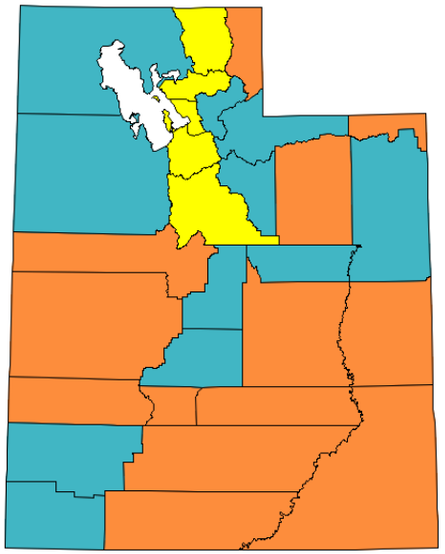
- **Most frequent substances** – opioid (7%), other (2.7%), cannabis (2.5%) amphetamine (0.9%),
- No difference in cord positivity by substance type and region



Substance		All	Urban	Rural	Frontier	p
Positive substance in cord panel						
	Opioid	122 (7.0)	109 (7.3)	10 (5)	3 (5)	0.257
	Other	48 (2.7)	44 (3.0)	2 (1)	1 (2)	0.203
	Amphetamine	16 (0.9)	13 (0.9)	2 (1)	1 (2)	0.575
	Benzodiazepine	10 (0.5)	8 (0.5)	1 (1)	0 (1)	0.875
	Cocaine	1 (0.1)				
	THC-COOH (Cannabis)	43 (2.5)	34 (2.3)	6 (3)	3 (5)	0.07
	Alcohol (Ethyl Glucuronide)	7 (0.4)	6 (0.4)	1 (0)	0 (0)	0.891

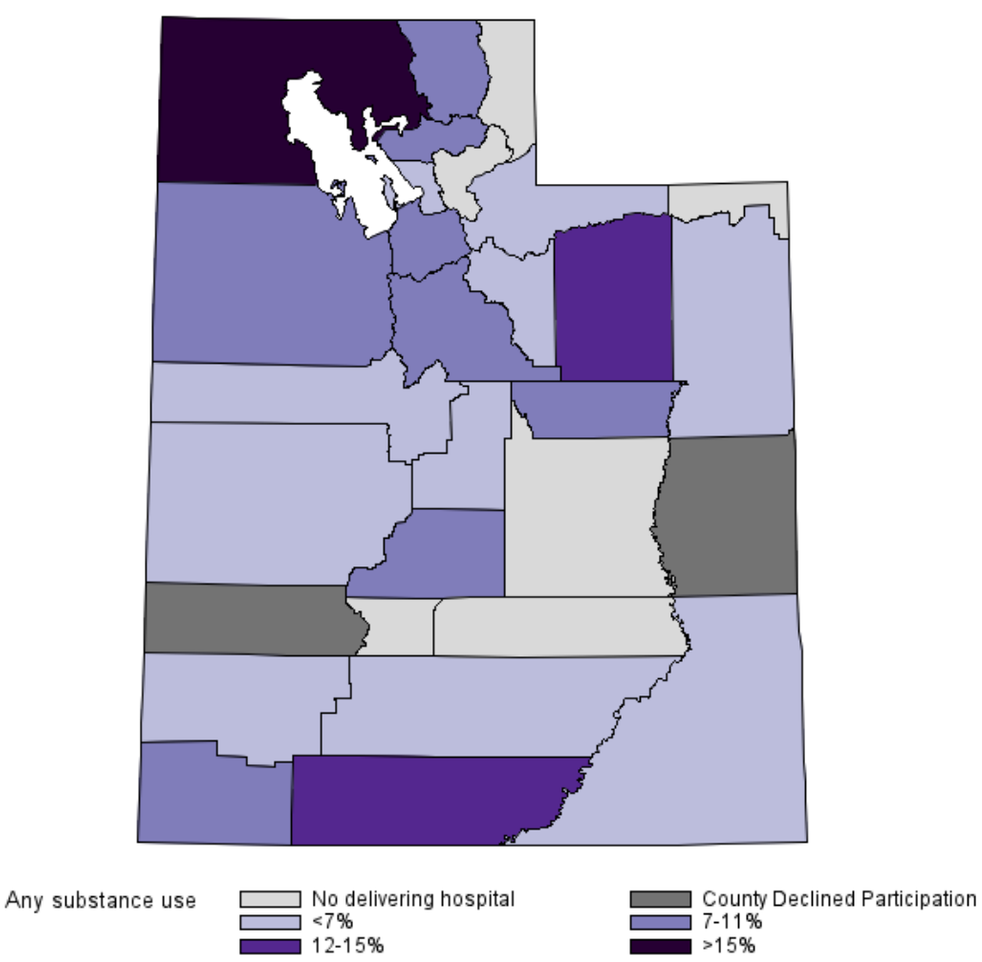
RESULTS

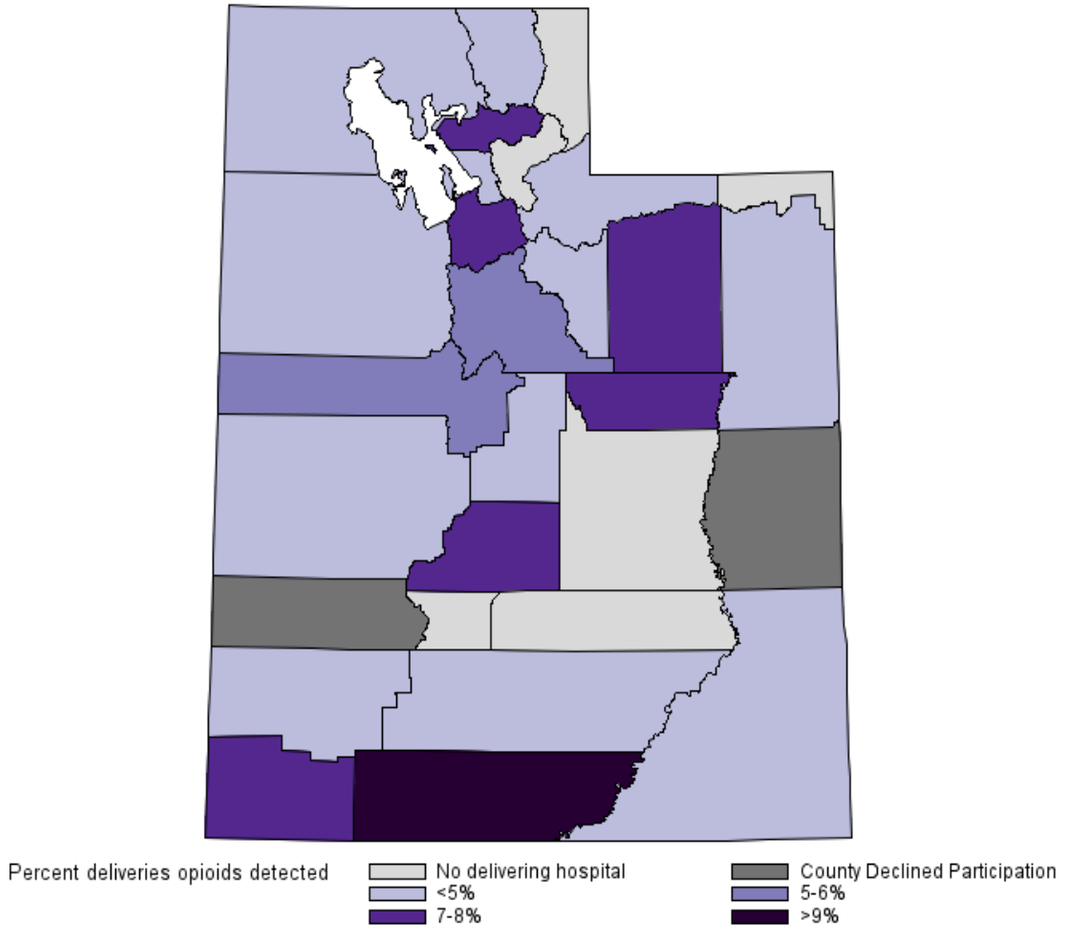
- **1.2% cords positive** for multiple substance types
- All cords with multiple substances (n=21) were opioid positive



Substance		All	Urban	Rural	Frontier	p
	Unweighted N	**1748**	988	384	376	
	Weighted N	**1748**	1495	197	56	
Number of Substances in cord	0	1575 (90.1)	1341 (89.7)	183 (93)	51 (91)	0.347
	1	152 (8.7)	135 (9.0)	13 (6)	5 (9)	
	2*	18 (1.1)	19 (1.3)	1 (1)	0 (0)	
	3	3 (0.1)				

RESULTS





County prevalence for **any substance** cord positivity ranges 0-15.8%

County prevalence for **opioid positivity** ranges 0-13.3%

COMPARED TO HISTORICAL RESULTS

Characteristic	Varner	Smid	P	
	N=850	N=1748		
Any substance use	58 (6.8)	173 (9.9)	0.013	45% increase
Opioid	40 (4.7)	122 (7.0)	0.03	48% increase
THC-COOH	4 (0.5)	43 (2.5)	<.001	400% increase
Ethyl Glucuronide	3 (0.4)	7 (0.4)	0.887	
Amphetamine	1 (0.1)	16 (0.9)	0.01	800% increase
Cocaine	1 (0.1)	1 (0.1)	0.819	

The Prevalence of Prenatal Opioid and Other Drug Use in Utah

Karen F. Buchi, MD [1] Carla Suarez, BS [1] Michael W. Varner, MD [2]

CONCLUSIONS

- Nearly **one in ten pregnant individuals in Utah** have prenatal substance use based on positive cord assay

- Prenatal substance use in Utah **increased 48%** over past decade
  - Driven by opioids, amphetamine and cannabis

- Anonymous collection of cord samples is a **viable** option for statewide surveillance of prenatal substance use

WHAT NEXT?

- Suicides and drug-related deaths are increasingly prevalent in the US
  - Preventability is hinged on identification and treatment.

- Pregnancy-related ness is KEY question for pregnancy and suicide deaths.
  - Understanding pregnancy and its role in these deaths will help with identification and treatment.

- Anonymous Umbilical cord prevalence studies may help with surveillance
  - Screening helps on patient level but may need different system for true prevalence.


Thank you!
Additional Questions?
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