REGULAR ARTICLE

ACTA PÆDIATRICA
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Factors associated with age of death in sudden unexpected infant death

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Abstract

Aim: This study aimed to systematically analyse the pregnancy, birth and demographic-related factors associated with age of death in sudden unexpected infant death (SUID).

Methods: Data were analysed from the Centers for Disease Control and Prevention's Cohort Linked Birth/Infant Death data set (2011-2013; 11 737 930 live births). SUID was defined as deaths from sudden infant death syndrome, ill-defined causes, or accidental suffocation and strangulation in bed. There were 9668 SUID cases (7-364 days; gestation >28 weeks; 0.82/1000 live births). The odds of death at different ages were compared to determine which variables significantly affect the SUID age of death.

Results: Forty-three features indicated a significant change in age of death with two main patterns: (a) younger chronologic age at death was associated with maternal smoking and factors associated with lower socio-economic status, and (b) older age was associated with low birthweight, prematurity and admission to the neonatal intensive care unit. However, when age was corrected for gestation, these factors were associated with younger age.

Conclusion: Factors that varied with age of death are well-documented risk factors for SUID. The majority of these risk factors were associated with younger age at death after allowing for gestational age at birth.

KEYWORDS
SIDS, sudden infant death, SUID

1 | INTRODUCTION

Sudden unexpected infant death (SUID) is a broad term that describes the death of an infant (<365 days of age) that occurs suddenly and unexpectedly, and the cause is not obvious before investigation. It includes three causes of death as classified by the *International Classification of Diseases, 10th Revision* (ICD-10): sudden infant death syndrome (SIDS, R95), ill-defined causes (R99) and accidental

suffocation and strangulation in bed (W75) which, combined, result in approximately 3700 deaths annually in the United States.[1]

The age distribution of SUID is well described and unique, with relatively small numbers in the first month of life, a peak at 2-3 months and approximately 90% of deaths occurring before 6 months of age. This age distribution is often referred to as a critical developmental age.[2] While this is the least studied of the three SIDS risk areas proposed in Filiano and Kinney's Triple Risk

Model in 1994, developments in age-related changes have been shown in REM sleep architecture,[3] as well as arousal responses to hypoxia in SIDS infants [4] and anoxia responses in mouse models with brainstem serotonin deficiencies.[5] A weak hypoxia response has also been reported at a critical period of respiratory development in rat models.[6]

The risk of SUID with bed-sharing has been shown to be higher in young infants, especially those less than 3 months of age,[7] whereas older infants were more likely to change from side/back to prone.[8] Both these findings are consistent with the motor skills of infants; young infants lack the motor skill to move away from an asphyxia threat while bed-sharing, whereas the developing motor skills in the older infant enables them to move from the side position to the prone position.

Two studies from the late 1980s reported that risk factors differ by age at death.[9,10] In one study, age at death was greater in infants born with low birthweight.[9] This study also found a higher median age at death for babies born in summer than in winter. The other study reported that young mothers and smoking in pregnancy were associated with higher risk in the first months of life.[10] The authors concluded that this was evidence for different causes of SIDS with different distributions according to age at death.

There has been no systematic analysis of pregnancy, birth and demographic-related factors associated with the age at death in SUID. The aim of this study was to rectify this deficiency. The study is hypothesis-generating, and thus we examined all potential risk factors for SUID available in the Centers for Disease Control and Prevention's (CDC) Cohort Linked Birth/Infant Death data set.

2 | METHODS

2.1 | Data source

The study uses data from the CDC's Cohort Linked Birth/Infant Death data set for births between 2011 and 2013.[11]

2.2 | Case definition

Sudden unexpected infant death was defined as deaths from sudden infant death syndrome (SIDS, R95), ill-defined causes (R99) or accidental suffocation and strangulation in bed (W75). SUID in the early neonatal age group (<7 days),[12] deaths over one year of age and infants born before 28 weeks gestation were excluded. The data set reports deaths up to one year of age; thus, there is no information on deaths in the second year of life.

2.3 | Control definition

Controls were infants born at 28 weeks of gestation or later who survived their first year.

> **Key notes**
>
> - Approximately 11 million live births and 10 000 SUID cases were analysed to determine risk factors that significantly affect the age of death due to sudden unexpected infant death (SUID) in the United States.
> - The majority of demographic, prenatal and infant risk factors were associated with younger gestation-corrected age.
> - These data provide potential clues for the physiological mechanisms underlying SUID.

2.4 | Explanatory variables

In total, there are 244 multi-valued fields available in the CDC data set which include information regarding demographics, labour and delivery, pregnancy care, smoking, obstetric procedures and neonatal tests after birth. Many of these fields record similar information in slightly different formats—for example bucketed or not—and many fields are flags for meta-information—for example data imputed or not. In the univariate analysis, 74 of these 244 multi-valued fields were analysed, eliminating fields which encoded meta-information and choosing one of several possible bucket sizes in most cases. All values of included fields were encoded as binary factors, where values listed as 'unknown' or that were blank were encoded in the same manner as known values so that the effects of missing/unknown data could be included in the analysis. Variables where the population size was less than 20, in either cases or controls, were excluded. This resulted in 352 binary-encoded attributes of each SUID infant.

2.5 | Statistical analysis

We first performed a univariate analysis comparing the age of death distributions across the set of all SUID infants for the two binary values (yes/no). We tested null hypotheses of the form 'The distribution of age of death of infants due to SUID who had attribute X is not different from the distribution of age of death due to SUID who did not have attribute X'. The granularity of age of death in days allows us to compare distributions directly rather than relying on predetermined age buckets as previous studies have done.[10] Because the age of death does not follow a normal distribution, p-values were calculated using the Mann-Whitney U test (Python 3.7.1, SciPy 1.1.0, Statsmodels 0.9.0). To control for multiple testing, the Benjamini-Hochberg procedure was used to control false discovery rate and only attributes with an adjusted P-value < 0.05 were considered indicative of a significant change in the age of death due to SUID.[13] Secondly, an analysis was undertaken using age corrected for gestation (postmenstrual age—280 days; subsequently referred to as corrected age) rather than chronological age.

Logistic regression models were used to understand how odds of SUID change with infant age while controlling for feature interaction. Models were developed to predict death at each completed month of age (0-4 and 5+) using all SUID cases from each month compared to a 20 times larger sample chosen at random from the controls. Because SUID is such a rare event (0.082%), if the model used all the data to learn 'SUID' versus 'not SUID', it would likely learn to predict 'not SUID' on every data point. Such a model would have an accuracy of 99.918%. In cases of such extreme class imbalance, it is common to down-sample the majority class to achieve a better predictive behaviour and reliable adjusted odds ratios (aORs).

Regression analysis and structure learning were used to understand variable interaction and decrease bias in the models. Structure learning was performed using a Bayesian network, a type of probabilistic graphical model,[14] to gain an estimate of which variables in the set of possible features are directly associated with SUID and with age of death. Regression analysis was used to further enrich the feature set to maximise performance of the regression model. On the basis of these calculations, the following covariates were used in most models: age, race, education, marital status, maternal body mass index (BMI, weight (kg)/height (m)^2), smoking before and during pregnancy, admission to neonatal intensive care unit (NICU), birthweight, birth order, interval since last live birth, breech birth, 5-minute Apgar score and whether or not the infant was born via C-section. For some models, a variable was not included in the model when there was collinearity between two similar variables, for example smoking before pregnancy and smoking in pregnancy.

3 | RESULTS

In the 3-year study, there were 11 737 930 live births and 9668 deaths from SUID in the postperinatal period with gestation 28 weeks or more (rate 0.82/1000 live births). The overall distribution by individual ICD-10 code included 49% R95, 29% R99 and 22% W75. However, the distribution of R95, R99 and W75 varies significantly by state (chi-square statistic = 1823, df = 60, P < 0.00001, which is based on 31 states which did not have any suppressed values for R95, R99 and W75; values between 0 and 9 are suppressed) (Table S1).[15] Therefore, to capture all SUIDs and minimise the effect of variation in coding across US states, all additional analyses combined the three cause of death codes into a single SUID category.

The distribution of all SUID showed an overall mean age of death of 103 days and a median age of death of 86 days. Mean corrected age of death was 93 days and median corrected age of death 77 days. Figure 1 compares the age of death for chronological age and corrected age. Although the median age is different, the skewness and dispersion are similar.

From the multiple hypothesis testing analysis, there were 43 individual features in 23 different fields that revealed a statistically significant difference in distribution of age of death compared to the rest of the SUID population with two main patterns:
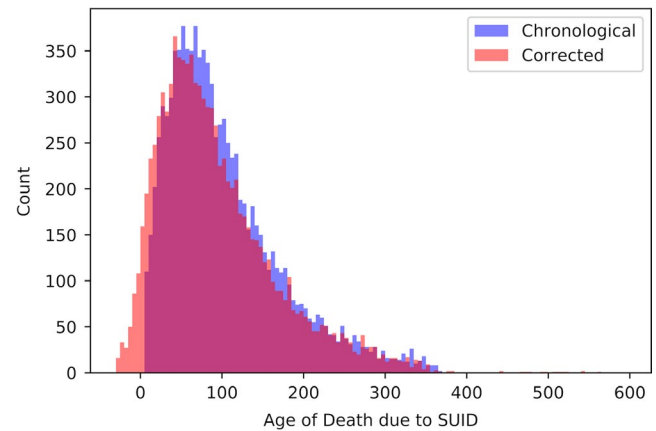
FIGURE 1 Comparison of chronological age of death with corrected age of death due to SUID, 2011-2013. SUID, sudden unexpected infant death

3.1 | Smoking, socio-economic status and race

Mothers reporting smoking in the three months before pregnancy as well as those smoking during pregnancy were associated with a younger age of death compared with mothers that did not smoke (Table 1). Non-smokers were associated with an older age of death compared to all other SUID cases. In general, the greater the average number of cigarettes smoked during pregnancy, the younger the median age of death of the infant (nil cigarettes/day = 90 days; 1-4 = 85 days; 5-9 = 76 days; 10-19 = 74 days and 20+ = 80 days).

Factors generally associated with more advantaged socio-economic status correlated with an older age of death on average for both chronological age and corrected age (Table 1). For example, mothers who had a higher education degree including a bachelor's or master's degree, fathers who had a bachelor's degree, mothers who were married at the time of the child's birth, breastfeeding and having private insurance correlated with a significantly older age of death compared to the rest of the SUID population. In contrast, factors often correlated with disadvantaged socio-economic status, including a high maternal BMI (≥35), unmarried mothers at the time of birth, father's age is unknown or recorded as 'not stated' on the birth certificate, Medicaid insurance, participation in the WIC (Supplemental Nutrition Program for Women, Infants, and Children) programme, diagnosis of hepatitis C and starting prenatal care in the third trimester were associated with a younger age of death. Outside of this trend, those with no insurance and infants with a sibling 12-17 months older correlated with an older age of death.

Race was found to be another important determinant of the age of death (Table 1). Father's race being stated as 'unknown' on the birth certificate or mother's race stated as black was significantly correlated with a younger age of death. Father's race stated as either white or Hispanic, and mother's race stated as Hispanic were associated with an older age of death.

Infants with a sibling 12-17 months older stand out as the only risk factor correlated with an older age at death for both chronological age and corrected age.

TABLE 1 List detailing chronological age vs corrected age at death for maternal, paternal, pregnancy and infant factors

	n	Chronological age at death				Corrected age at death			
		P-value	Pass sig. test	Median age of death	Older or younger	P-value	Pass sig. test	Median age of death	Older or younger
Maternal factors									
Maternal education: 9th-12th grade (no diploma)	2106	<0.01	TRUE	81	Younger	<0.001	TRUE	70	Younger
Maternal education: Bachelor's degree	493	<0.001	TRUE	102	Older	<0.001	TRUE	95	Older
Maternal education: Master's degree	143	<0.001	TRUE	110	Older	<0.001	TRUE	103	Older
Maternal education: High school graduate	6047	<0.05	FALSE	86	Older	<0.01	TRUE	78	Older
Maternal Education: Not a high school graduate	3621	<0.05	FALSE	84	Younger	<0.01	TRUE	74	Younger
Mother's Race: Black	2815	<0.01	TRUE	83	Younger	<0.001	TRUE	71	Younger
Mother's Race: Hispanic	928	<0.001	TRUE	93	Older	<0.001	TRUE	86	Older
BMI = 35.0-39.9: Obesity	650	<0.001	TRUE	75	Younger	<0.01	TRUE	67	Younger
BMI ≥ 40: Extreme obesity	561	<0.01	TRUE	76	Younger	<0.01	TRUE	67	Younger
Married	3067	<0.001	TRUE	91	Older	<0.001	TRUE	83	Older
Unmarried	6601	<0.001	TRUE	83	Younger	<0.001	TRUE	74	Younger
Not a WIC recipient	2845	<0.001	TRUE	89	Older	<0.05	FALSE	80	Older
WIC recipient	5350	<0.01	TRUE	83	Younger	<0.05	FALSE	74	Younger
Did not smoke before pregnancy	6895	<0.001	TRUE	89	Older	<0.001	TRUE	80	Older
Smoked before pregnancy	2773	<0.001	TRUE	78	Younger	<0.001	TRUE	69	Younger
Paternal Factors									
Father's age not stated	2948	<0.001	TRUE	82	Younger	<0.001	TRUE	71	Younger
Father's race: White	4233	<0.01	TRUE	88	Older	<0.001	TRUE	81	Older
Father's race: Unknown	3081	<0.01	TRUE	82	Younger	<0.001	TRUE	72	Younger
Father's race: Hispanic	175	<0.01	TRUE	100	Older	<0.01	TRUE	91	Older
Father's race: Black	1862	0.06	FALSE	83	Younger	<0.01	TRUE	73	Younger
Father's education: Bachelor's degree	334	<0.001	TRUE	100	Older	<0.001	TRUE	95	Older
Father's education: Unknown	2725	<0.05	FALSE	82	Younger	<0.001	TRUE	72	Younger
Pregnancy Factors									
Did not smoke during pregnancy	7180	<0.001	TRUE	88	Older	<0.001	TRUE	80	Older

(Continues)

TABLE 1 (Continued)

		Chronological age at death				Corrected age at death			
	n	P-value	Pass sig. test	Median age of death	Older or younger	P-value	Pass sig. test	Median age of death	Older or younger
Smoked during pregnancy	2488	<0.001	TRUE	77	Younger	<0.001	TRUE	67	Younger
Maternal hepatitis C positive	105	<0.01	TRUE	65	Younger	<0.01	TRUE	57	Younger
*Plurality: Singleton	9154	<0.01	TRUE	85	Younger	<0.001	TRUE	77	Older
*Plurality: Multiple	504	<0.01	TRUE	92	Older	<0.001	TRUE	64	Younger
Insurance: Private	1725	<0.001	TRUE	97	Older	<0.001	TRUE	88	Older
Insurance: Medicaid	5839	<0.001	TRUE	82	Younger	<0.001	TRUE	72	Younger
Insurance: Self-pay	253	<0.01	TRUE	99	Older	<0.05	FALSE	87	Older
Prenatal care began 7th-final month	644	<0.01	TRUE	77	Younger	0.48	FALSE	74	Younger
No prenatal care	302	0.68	FALSE	80	Younger	<0.05	FALSE	66	Younger
*Interval of last live birth: Plural delivery	174	0.11	FALSE	91	Older	<0.001	TRUE	59	Younger
Interval of last live birth: 12-17 mo	942	<0.001	TRUE	93	Older	<0.001	TRUE	83	Older
Interval of last live birth: 72+ mo	639	<0.05	FALSE	78	Younger	<0.01	TRUE	69	Younger
Weight gain: <11 lbs	1119	0.10	FALSE	83	Younger	<0.001	TRUE	72	Younger
*Delivery induced	2013	0.24	FALSE	85	Younger	<0.01	TRUE	82	Older
*Delivery not induced	7628	0.18	FALSE	86	Older	<0.01	TRUE	75	Younger
*No trial of labour attempted	2187	0.09	FALSE	87	Older	<0.01	TRUE	73	Younger
Total birth order: 2nd	2521	<0.05	FALSE	88	Older	<0.001	TRUE	82	Older
Total birth order: 7th	238	<0.05	FALSE	77	Younger	<0.001	TRUE	67	Younger
Live birth order: 2nd	2980	<0.01	TRUE	88	Older	<0.001	TRUE	80	Older
Live birth order: 3rd	2051	<0.05	FALSE	83	Younger	<0.01	TRUE	72	Younger
Steroids during labour and delivery	214	0.43	FALSE	87	Younger	<0.001	TRUE	49	Younger
No steroids during labour and delivery	8164	0.93	FALSE	85	Older	<0.01	TRUE	77	Older
Infant factors									
*5-min Apgar score: 7-8	1532	0.69	FALSE	86	Older	<0.001	TRUE	71	Younger
*5-min Apgar score: 9-10	7791	0.18	FALSE	85	Younger	<0.001	TRUE	78	Older
*Gestational age: 28-31 wk	323	<0.001	TRUE	106	Older	<0.001	TRUE	36	Younger
*Gestational age: 32-33 wk	326	0.11	FALSE	90	Older	<0.001	TRUE	42	Younger
*Gestational age: 34-36 wk	1426	0.46	FALSE	87	Older	<0.001	TRUE	58	Younger
Gestational age: 37-38 wk	2664	<0.01	FALSE	82	Younger	<0.001	TRUE	68	Younger

(Continues)

TABLE 1 (Continued)

	n	Chronological age at death				Corrected age at death			
		P-value	Pass sig. test	Median age of death	Older or younger	P-value	Pass sig. test	Median age of death	Older or younger
*Gestational age: 39 wk	2356	0.10	FALSE	83	Younger	<0.001	TRUE	79	Older
Gestational age: 40 wk	1384	<0.05	FALSE	90	Older	<0.001	TRUE	93	Older
*Gestational age 41 wk	606	0.71	FALSE	84	Younger	<0.001	TRUE	94	Older
*Gestational age: 42+ wk	566	0.33	FALSE	83	Younger	<0.001	TRUE	108	Older
*Birthweight: 750-999 g	39	<0.001	TRUE	143	Older	0.85	FALSE	80	Younger
*Birthweight: 1000-1249 g	68	<0.01	FALSE	104	Older	<0.001	TRUE	39	Younger
*Birthweight: 1250-1499 g	121	<0.001	TRUE	105	Older	<0.001	TRUE	56	Younger
*Birthweight: 1500-1999 g	465	0.15	FALSE	91	Older	<0.001	TRUE	53	Younger
Birthweight: 2000-2499 g	1138	<0.01	TRUE	80	Younger	<0.001	TRUE	61	Younger
Birthweight: 2500-2999 g	2470	<0.001	TRUE	78	Younger	<0.001	TRUE	69	Younger
Birthweight: 3000-3499 g	3332	0.39	FALSE	86	Older	<0.001	TRUE	82	Older
Birthweight: 3500-3999 g	1597	<0.05	FALSE	89	Older	<0.001	TRUE	88	Older
Birthweight: 4000-4499 g	357	<0.01	TRUE	94	Older	<0.001	TRUE	96	Older
Birthweight: 4500-4999 g	53	0.06	FALSE	105	Older	<0.01	TRUE	113	Older
*Newborn received antibiotics	298	<0.01	TRUE	98	Older	<0.01	TRUE	68	Younger
*Newborn received assisted ventilation	442	<0.05	FALSE	91	Older	<0.001	TRUE	66	Younger
*Newborn admitted to NICU	1189	<0.001	TRUE	95	Older	<0.001	TRUE	66	Younger
*Newborn not admitted to NICU	7172	<0.001	TRUE	84	Younger	<0.001	TRUE	78	Older
*Newborn received surfactant	60	<0.01	TRUE	117	Older	0.33	FALSE	74	Younger
Newborn not breastfed	3097	<0.001	TRUE	81	Younger	<0.001	TRUE	71	Younger
Newborn breastfed	4359	<0.001	TRUE	88	Older	<0.001	TRUE	80	Older

Note: Includes the full list of every feature that passed the significance test for chronological age, corrected age or both. 'Older or younger' indicates if the median age of death for a given factor is older/younger than the overall median chronological (84 d) or gestation-corrected (76 d) age of death. An * indicates factors in which younger or older reverses when chronological age is compared to corrected age. Pass sig test = TRUE means that the variable passed the Benjamini-Hochberg procedure with a *P*-value < 0.05. Variable descriptions: WIC = needs-based supplemental nutrition programme for Women, Infants, and Children; Medicaid = free or low-cost health coverage to eligible needy persons; Insurance: self-pay = paying for health care without insurance.

Abbreviation: BMI, body mass index; NICU, neonatal intensive care unit.

A

B

☐ Chronological Age   ■ Corrected Age
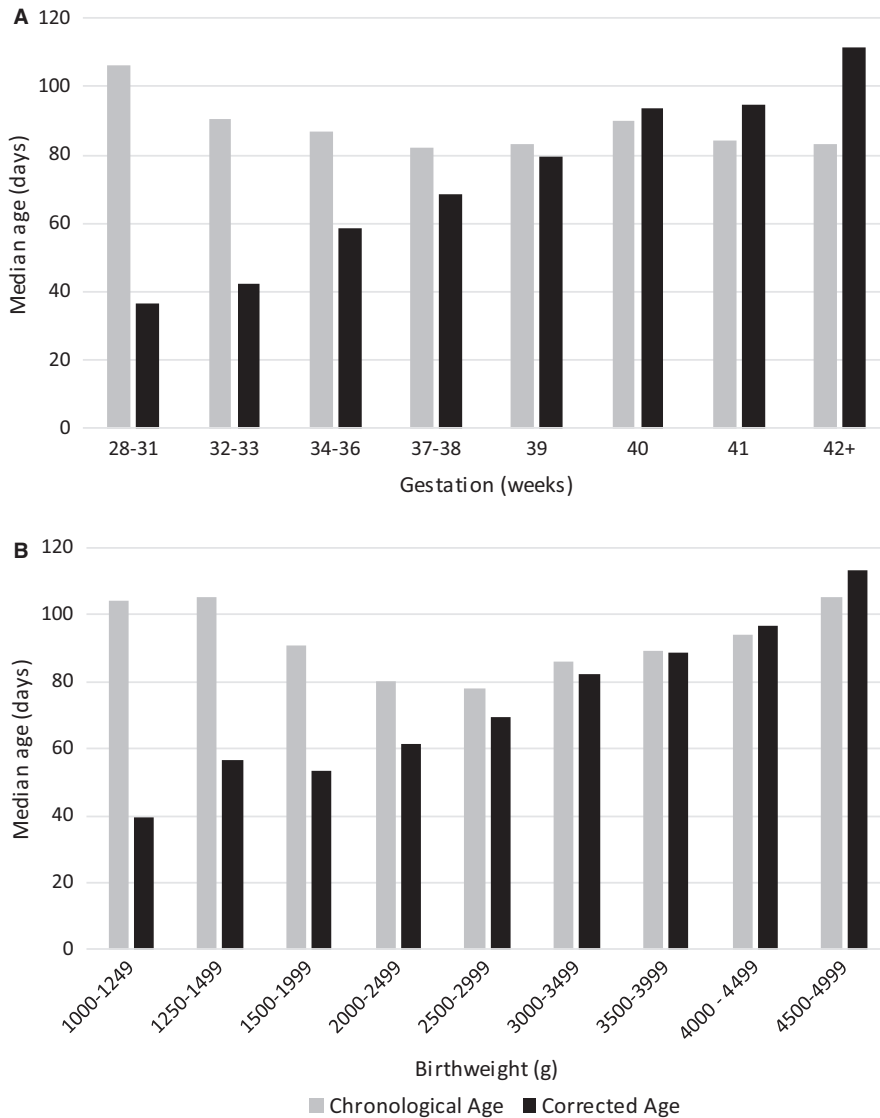
FIGURE 2 Median age of death comparing chronological age at death (grey) versus corrected age at death (postmenstrual age—280 d; black) by length of gestation (A) and birthweight (B)

3.2 | Complications of pregnancy and delivery, birthweight and gestation

Contrary to the effect of smoking, we found that factors that are generally consistent with low birthweight, prematurity and complications of pregnancy and birth were consistently correlated with a significantly older chronological age of SUID. These included very low birthweights (<1500 g), high birthweights (4000-4499 g), admission to the NICU, surfactant treatment after birth, administration of antibiotics at birth, gestational length between 28 and 31 weeks and twin births (Table 1). However, when the analysis was conducted using corrected age, the effect on complications of pregnancy and delivery, birthweight and gestation was reversed, that is they were associated with a younger age at death (Table 1). This is illustrated for gestation (Figure 2A) and birthweight (Figure 2B).

Sex of the infant and season of death stand out as the only well-known risk factors that did not have a statistically detectable difference in either chronological or corrected age of death (median

chronological age of death males = 86 days and females = 84 days, $P = 0.35$; summer = 88 days, winter = 84 days, $P = 0.09$).

3.3 | Risk of SUID by month of age

This multivariable analysis examined the risk of SUID by month of chronological age. The aOR of smoking during pregnancy is highest in the first month (days 7-30), and there is a nearly linear decline over the course of the first 5 months (Figure 3A). Smoking before pregnancy is still a risk when we control for smoking during pregnancy; however, it does not have a clear trend with age (Figure 3B).

There were progressive decreasing odds of SUID with increasing month of age for mothers with a high BMI (Figure 4A) and unmarried mothers (Figure 4B).

The aOR shows a clear positive correlation with increasing month of age for infants born with a low birthweight (<2500 g; Figure 5A), infants admitted to the NICU after birth (not shown) and infants with a sibling less than 18 months older (Figure 5B).
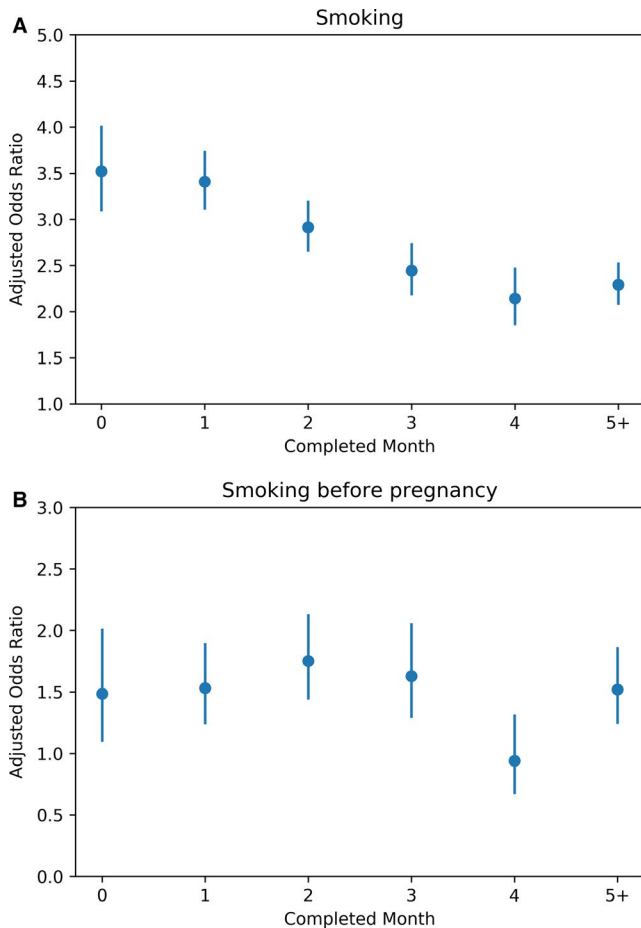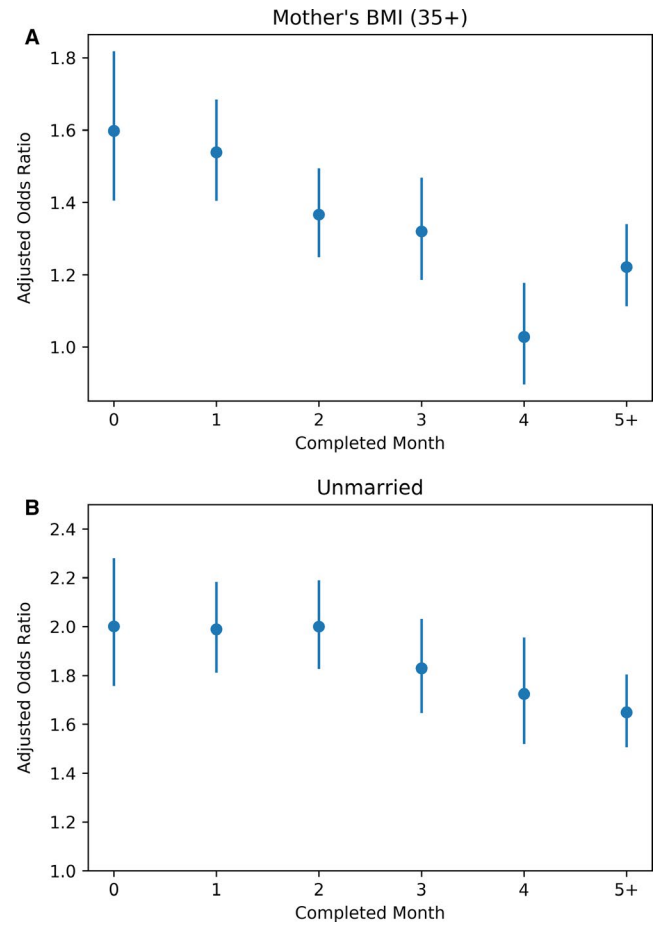
FIGURE 3 The adjusted OR of maternal cigarette smoking (A) during and (B) before pregnancy by month of age for SUID. Completed month 0 = days 7-30. SUID, sudden unexpected infant death

FIGURE 4 Adjusted OR of mother's BMI (35+) (A), marriage status (B). BMI, body mass index

4 | DISCUSSION

Sudden infant death syndrome (SIDS) is one cause of death under the term SUID. While SIDS rates have declined since the late 1990s, the combined SUID rate, which also includes unknown causes and accidental suffocation in bed, has remained relatively unchanged.[16] This suggests diagnostic transfer, or a shift in the classification of causes of death, a well-documented phenomenon.[17-19] For this reason, we included the three most commonly reported types of SUID (R95 + R99 + W75) in our analysis. In addition, we excluded cases that occurred in the first week of life as the epidemiology differs from that in the postperinatal period.[12]

This study examined risk factors that are available through the CDC. From hundreds of variables, 43 were found to be indicative of a significant change in the chronological age of a SUID. They could be largely grouped into two categories: (a) smoking during pregnancy and factors associated with disadvantaged racial categories and lower socio-economic status correlate with younger age of death, and (b) factors associated with complications of pregnancy and delivery, low or very high birthweight, and short gestation correlate with older chronological age of death; however,

after adjustment for gestation, these factors were associated with younger corrected age. This supports the contention that a baby born premature will pass through the vulnerable developmental window at a later postnatal age, because it was born at an earlier gestational age.

Identifying these larger trends in age of death distributions for different risk factors can help give important clues into the underlying mechanisms of SUID, and how they affect the timing of the deaths. More clinically relevant, however, is the assessment of relative risk over the first year of life for known risk factors. For example, it is well documented that there is a positive correlation between maternal smoking of cigarettes during pregnancy and an increased risk of SUID [20,21]; indeed, the relationship is thought to be causal.[22] Possible reasons for the association between in utero tobacco exposure and higher rates of SIDS/SUID in the first months of life include abnormalities in brain development,[23] which may result in reduced ventilatory responses to hypoxia,[24] disturbed cardiorespiratory control and arousal mechanisms,[25] and/or abnormal pulmonary development.[26] While there is still an elevated risk compared to non-smokers, the risk of SUID due to smoking decreases almost linearly until about 5 months. This underscores the importance of smoking cessation before pregnancy. Clearly, there exists a subset of cases in which the child

A

B
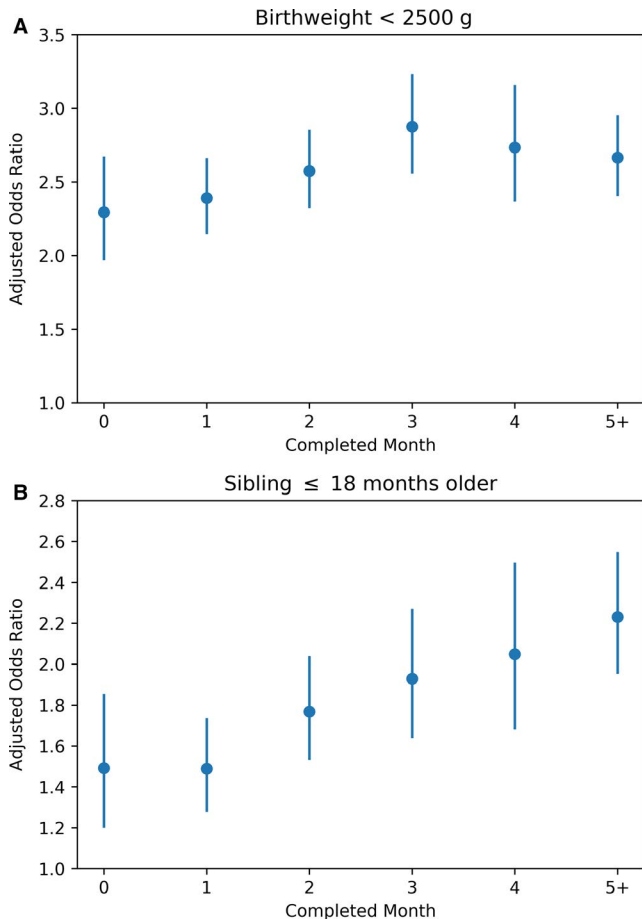
FIGURE 5 Adjusted OR for low birthweight (<2500 g; A) and siblings ≤18 mo older (B) for SUID. Completed month 0 = days 7-30. SUID, sudden unexpected infant death

was not exposed to tobacco that tended to die at a later age, suggesting distinct mechanistic causes of SUID between exposed and non-exposed infants to nicotine in utero.

It is well established that low socio-economic status is a risk factor for SIDS/SUID.[27,28] The CDC data do not provide a direct measurement of income; however, low education and several factors (such as starting prenatal care in the 3rd trimester or Medicaid insurance) associated with lower socio-economic status correlated with a younger age of death. In contrast, factors generally associated with a higher socio-economic status (such as parents with higher education or private insurance) correlated with older SUID. Two factors with clear trends showing an elevated SUID risk in the first 1-2 months after birth were an elevated maternal BMI and unmarried mothers. Future investigative studies could explore potential distinct mechanistic factors that contribute to SUID between polarised socio-economic statuses.

The majority of SUID risk factors were associated with younger corrected age of death, and protective factors are associated with older corrected age. This is in keeping with the higher risk of SUID with bed-sharing in younger infants. However, there were three notable exceptions. First, although male infants are at higher risk of SUID than female infants, the age of death distributions did not differ. Second, in contrast to an earlier report the age of death did

not differ by season, despite the risk of SUID being higher in winter. Finally, a short interval since the last live birth is a risk factor for SUID and is associated with low socio-economic status.[29] We would have expected that this would be associated with younger age at death, but we found it associated with older corrected age of death. This is the only variable that showed this pattern, and the finding is unexplained.

Overall, these findings are meant to be hypothesis-generating. It is a limitation that our data source only includes variables available up to the point at which the newborn is discharged from the hospital after birth. We were unable to examine postnatal risk factors, especially those relating to infant care practices. However, major strengths of the study include the large sample size and the fact that data are collected prospectively and, therefore, not subject to recall bias.

The findings of this study support the hypothesis that there are multiple underlying mechanisms that may affect the vulnerable developmental window of the infant and time of SUID. Assuming that similar circumstances, such as hypoxic conditions, failed arousal and a certain developmental stage, render a child vulnerable to SUID, risk factors could influence the time window when these conditions come together.

It is striking that none of the individual risk factors in the multivariate analysis show the characteristic SUID curve for risk with age, indicating that the classic shape could be a product of some risk factors increasing and some decreasing with age. Because key risk factors increase/decrease with postnatal age and some can even be modified before pregnancy (eg BMI, smoking), it is important for healthcare providers to stress the importance of modifying known risk factors as well as educate about safe sleep in prenatal care visits. In populations with a high early risk of SUID (eg smokers and socio-economically disadvantaged families), it is especially important for healthcare providers to have early discussions about healthy sleep, and in populations where the risk is higher in infants older than the typical risk window, such as premature infants or short inter-pregnancy interval, it is worthwhile to message safe sleep practices for longer than may be necessary in the general population.

CONFLICTS OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.