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,\(^2\) 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.\(^5\)

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.

### 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 9,668 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:

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.
| Maternal factors                                                                 | 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 |
|---------------------------------------------------------------------------------|-----|---------|----------------|---------------------|-----------------|---------|----------------|---------------------|-----------------|
| 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 | n | P-value | Pass sig. test | Median age of death | Older or younger |
|---|---|---|---|---|---|---|---|---|---|
| Smoked during pregnancy | 2488 | <0.001 | TRUE | 77 | Younger | 2488 | <0.001 | TRUE | 67 | Younger |
| Maternal hepatitis C positive | 105 | <0.01 | TRUE | 65 | Younger | 105 | <0.01 | TRUE | 57 | Younger |
| *Plurality: Singleton | 9154 | <0.01 | TRUE | 85 | Younger | 9154 | <0.01 | TRUE | 77 | Younger |
| *Plurality: Multiple | 504 | <0.01 | TRUE | 92 | Older | 504 | <0.01 | TRUE | 64 | Younger |
| Insurance: Private | 1725 | <0.001 | TRUE | 97 | Older | 1725 | <0.001 | TRUE | 88 | Older |
| Insurance: Medicaid | 5839 | <0.001 | TRUE | 82 | Younger | 5839 | <0.001 | TRUE | 72 | Younger |
| Insurance: Self-pay | 253 | <0.01 | TRUE | 99 | Older | 253 | <0.05 | FALSE | 87 | Older |
| Prenatal care began 7th-final month | 644 | <0.01 | TRUE | 77 | Younger | 644 | 0.48 | FALSE | 74 | Younger |
| No prenatal care | 302 | 0.68 | FALSE | 80 | Younger | 302 | <0.05 | FALSE | 66 | Younger |
| *Interval of last live birth: Plural delivery | 174 | 0.11 | FALSE | 91 | Older | 174 | <0.001 | TRUE | 59 | Younger |
| Interval of last live birth: 12-17 mo | 942 | <0.001 | TRUE | 93 | Older | 942 | <0.001 | TRUE | 83 | Older |
| Interval of last live birth: 72+ mo | 639 | <0.05 | FALSE | 78 | Younger | 639 | <0.01 | TRUE | 69 | Younger |
| Weight gain: <11 lbs | 1119 | 0.10 | FALSE | 83 | Younger | 1119 | <0.001 | TRUE | 72 | Younger |
| *Delivery induced | 2013 | 0.24 | FALSE | 85 | Younger | 2013 | <0.01 | TRUE | 82 | Older |
| *Delivery not induced | 7628 | 0.18 | FALSE | 86 | Older | 7628 | <0.01 | TRUE | 75 | Younger |
| *No trial of labour attempted | 2187 | 0.09 | FALSE | 87 | Older | 2187 | <0.01 | TRUE | 73 | Younger |
| Total birth order: 2nd | 2521 | <0.05 | FALSE | 88 | Older | 2521 | <0.001 | TRUE | 82 | Older |
| Total birth order: 7th | 238 | <0.05 | FALSE | 77 | Younger | 238 | <0.001 | TRUE | 67 | Younger |
| Live birth order: 2nd | 2980 | <0.01 | TRUE | 88 | Older | 2980 | <0.001 | TRUE | 80 | Older |
| Live birth order: 3rd | 2051 | <0.05 | FALSE | 83 | Younger | 2051 | <0.01 | TRUE | 72 | Younger |
| Steroids during labour and delivery | 214 | 0.43 | FALSE | 87 | Younger | 214 | <0.001 | TRUE | 49 | Younger |
| No steroids during labour and delivery | 8164 | 0.93 | FALSE | 85 | Older | 8164 | <0.001 | TRUE | 77 | Older |

**Infant factors**

| n | P-value | Pass sig. test | Median age of death | Older or younger |
|---|---|---|---|---|
| *5-min Apgar score: 7-8 | 1532 | 0.69 | FALSE | 86 | Older | 1532 | <0.001 | TRUE | 71 | Younger |
| *5-min Apgar score: 9-10 | 7791 | 0.18 | FALSE | 85 | Younger | 7791 | <0.001 | TRUE | 78 | Older |
| *Gestational age: 28-31 wk | 323 | <0.001 | TRUE | 106 | Older | 323 | <0.001 | TRUE | 36 | Younger |
| *Gestational age: 32-33 wk | 326 | 0.11 | FALSE | 90 | Older | 326 | <0.001 | TRUE | 42 | Younger |
| *Gestational age: 34-36 wk | 1426 | 0.46 | FALSE | 87 | Older | 1426 | <0.001 | TRUE | 58 | Younger |
| Gestational age: 37-38 wk | 2664 | <0.01 | FALSE | 82 | Younger | 2664 | <0.001 | TRUE | 68 | Younger |
|                                     | 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 |
| *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.
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).
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. This suggests diagnostic transfer, or a shift in the classification of causes of death, a well-documented phenomenon. 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.

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; indeed, the relationship is thought to be causal. 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, which may result in reduced ventilatory responses to hypoxia, disturbed cardiorespiratory control and arousal mechanisms, and/or abnormal pulmonary development. 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...
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. 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. 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.

ACKNOWLEDGEMENTS
We would like to thank Juan Lavista Ferres, Shirley You Ren, Vincent Chan, Richard Johnston, Avleen Bijral, Xiaohan Yan, Amit Misra and John Thompson for statistical guidance and useful discussion. A special thank you to John and Heather Kahan for inspiring this collaboration.

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.

How to cite this article: Allen K, Anderson TM, Chajewska U, Ramirez J-M, Mitchell EA. Factors associated with age of death in sudden unexpected infant death. Acta Paediatr. 2021;110:174–183. https://doi.org/10.1111/apa.15308