

# Circadian variation in sudden unexpected infant death in the United States

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## Abstract

**Aim:** To determine which factors are associated with sudden unexpected infant death (SUID) by time of day.

**Methods:** Data were analysed from the National Fatality Review Case Reporting System (2006-2015). Out of 20 005 SUID deaths in 37 states, 12 191 (60.9%) deaths had a recorded nearest hour of discovery of the infant. We compared distribution patterns between time of death and 118 variables to determine which were significantly correlated with SUID time of death using advanced statistical modelling techniques.

**Results:** The 12-hour time periods that were most different were 10:00 to 21:00 (daytime) and 22:00 to 09:00 (nighttime). The main features that were associated with nighttime SUID were bed sharing, younger infants, non-white infants, placed supine to sleep and found supine, and caregiver was the parent. Daytime SUID was associated with older infants, day care, white infants, sleeping in an adult bed and prone sleep position. Factors not associated with time of death were sex of the infant, smoking and breastfeeding.

**Conclusion:** Sudden unexpected infant death deaths that occur at night are associated with a separate set of risk factors compared to deaths that occur during the day. However, to minimise risk, it is important to practice safe sleep guidelines during both nighttime and daytime sleep.

## KEYWORDS

bed sharing, circadian rhythm, risk factors, sleep position, sudden unexpected infant death

## 1 | INTRODUCTION

Sudden unexpected infant death (SUID) is a term used to describe the sudden and unexpected death of a baby less than 1-year old in which the cause was not obvious before investigation.<sup>1</sup> These deaths would have previously been certified as sudden infant death syndrome (SIDS), but due to more detailed investigation, many of

these deaths are now labelled as accidental suffocation in a sleeping environment. Furthermore, certifying a cause of death in these cases is often subjective and dependent on the interpretation of a death scene and/or autopsy of a particular coroner or medical examiner. Diagnosis varies by jurisdiction and has changed over time. Annually, approximately 3600 deaths in the United States are due to SUID.

**Abbreviations:** NFR-CRS, National Fatality Review Case Reporting System; SIDS, sudden infant death syndrome; SUID, sudden unexpected infant death; XGBoost, Gradient boosted decision trees models.

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Most analyses of circadian variation in cases of sudden infant death have solely focused on SIDS, not SUID, cases. The majority of SIDS deaths occur at night<sup>2,3</sup> with a peak in the morning hours.<sup>4,5</sup> Night/morning deaths have been found to be associated with maternal smoking,<sup>2,4,6</sup> paternal smoking,<sup>3</sup> maternal alcohol consumption,<sup>2,4</sup> reported illness in the infant,<sup>2,4</sup> side or supine sleep position,<sup>4</sup> bed sharing<sup>2</sup> and single mothers.<sup>2</sup> Deaths that occur during the day/evening have mainly been associated with a prone sleep position.<sup>2,3,6</sup>

There are differences between day and night sleep that could result in disparate diurnal pathogeneses in cases of sudden infant deaths. Several theories have been posed as to why risk factors differ between day and nighttime SIDS including altered patterns of circadian rhythm,<sup>5,7</sup> abnormal sleep<sup>8,9</sup> and a reduction of melatonin synthesis.<sup>10</sup>

Many of the previous studies comparing risk factors to time of death were completed before the Back to Sleep campaigns in the early 1990s that led to a significant decrease in SIDS/SUID rates. In addition, sample sizes for the studies above were limited to only a few hundred cases and nearly every study was conducted in countries outside of the United States. As the deaths are rarely observed, the exact time of death is often difficult to estimate.

This study utilises advanced modelling techniques to analyse over 20 000 SUID cases between 2006 and 2015 in the United States to identify which variables significantly correlate with time of death.

## 2 | METHODS

### 2.1 | Data source

The data set was provided by the National Fatality Review Case Reporting System (NFR-CRS). It includes 20 005 infant deaths across 37 states between 2006 and 2015 where the Child Death Review team indicated primary cause of death to be asphyxia, injury-undetermined, injury-unknown, SIDS, medical-undetermined or medical-unknown. All these deaths were considered to be SUID and are the subject of this study.

We excluded infants that were born at <28 weeks' gestation. This exclusion avoids misclassification due to preterm birth.

### 2.2 | Outcome variable

Reported time of discovery to the nearest hour (1-12, AM/PM). For the purpose of this paper, these times have been converted to the 24-hour clock.

### 2.3 | Explanatory variables

There were 118 explanatory variables. Variables relevant to this report are as follows: age (days, categorised 0-59, 60-120 and 121+), birthweight, gestation, multiple birth, primary caregiver (parent vs. not parent), infant race (white vs. non-white), sex of infant, prenatal

### Key Notes

- Sudden unexpected infant deaths (SUID) peak at night.
- The 12-hour time period that was most different was 10:00 to 21:00 (daytime) and 22:00 to 09:00 (nighttime). SUID deaths that occur at night are associated with a separate set of risk factors compared to deaths that occur during the day.
- To minimise risk, it is important to practice safe sleep guidelines during both nighttime and daytime sleep.

care provided, cigarette smoking before pregnancy, cigarette smoking during pregnancy, infant breastfed, place of death (home, relative or friend's home, day-care centre or home, foster care home, hospital, other = hotel, baby sitter, shelter, outside, Indian reservation, public buildings, other specified categories, not specified and unknown), death related to sleep environment (specific question answered by child death review: 'Was the death related to sleeping or the sleep environment?'), sleeping place (crib, bassinet, adult bed, other), bed sharing (sleeping on same surface with person or animal), state (included in model, but not reported because of privacy concerns), position infant placed to sleep (back, stomach, side or unknown), position found (back, stomach, side or unknown) and sleeping on the floor.

### 2.4 | Statistical analysis

We only used data in the model where sample size was at least  $n = 30$ . In the case of numeric data, missing data were imputed as the median value of the feature; and in the case of categorical data, 'missing' was encoded as its own category.

Those cases with missing time of death were compared to those with this data.

The data were used to determine which two 12-hour periods of time most differentiated SUID cases, using statistical models and the feature set described above. To ensure that results were consistent, we developed both logistic regression models and gradient boosted decision trees models (XGBoost). Gradient boosted decision trees are an ensemble model of decision trees whose optimisation algorithm often results in better model performance compared to logistic regression, as it does in this case. However, the model is inherently non-linear, which prevents us from using it to calculate adjusted odds ratios. Having a logistic regression model that agrees with the XGBoost model on the daytime/nighttime split and mostly agrees on the list of predictive variables gives us greater confidence in the results and allows us to calculate reliable adjusted odds ratios. All logistic regression and XGBoost models were adjusted for covariates, and model performance was evaluated using macro-average F1 score and 5-fold cross-validation.

To understand the features most correlated with daytime and nighttime SUID, we used the SHAP TreeExplainer method<sup>11,12</sup> while

accounting for all covariates in our best-performing XGBoost model. The SHAP TreeExplainer method is a state-of-the-art algorithm for producing model explanations for tree-based models that relies on the theoretically optimal Shapley values for feature importance.

### 3 | RESULTS

In the NCFRP case registry, there were 20 005 SUID deaths. Of these, 12 191 (60.9%) deaths had a recorded nearest hour of discovery of the infant. These deaths are the subject of this study. Distribution pattern of the reported time of death/found is shown in Figure 1.

Cases with a reported time of death are less likely to be bed sharing (63% vs. 72%,  $p < 0.05$ ), less likely to have maternal smoking at any time during pregnancy (53% vs. 55%,  $p = 0.036$ ), and have a slightly older mean age of primary caregiver (25.7 years vs. 25.4 years,  $p < 0.05$ ). Cases with/without reported time of death are not statistically differentiable ( $p > 0.05$ ) for birthweight, infant age and the likelihood that the primary caregiver is the biological mother.

All 12 possible divisions of the day into distinct 12-hour intervals were analysed, and the time periods which were most differentiable using our statistical models were 22:00 to 09:00 and 10:00 to 21:00 (hereafter referred to as 'nighttime' and 'daytime', respectively). The 5-fold f1 score for the models predicting 22:00-09:00 and 10:00-21:00 was 0.67 for the XGboost model and 0.66 for the logistic regression model. This is compared to f1 scores of 0.41 and 0.42, respectively, for the pair of times which were least statistically differentiable (05:00-16:00 vs. 17:00-04:00). There were 4752 (39.0%) deaths in daytime and 7439 (61.0%) at night.

After controlling for all features in the dataset, both XGBoost and logistic regression models showed that the factors that were most associated with nighttime SUID included bed sharing, younger infants, non-white infants, placed supine to sleep and found in supine position, and caregiver was the parent (Table 1). The findings for age of infant and time of death are shown in Figure 2 (continuous) and Figure 3 (categorised). In both the XGboost and logistic

regression models, bed sharing was the feature most strongly associated with time of death, followed by infant age, as determined by mean absolute value of the SHAP values for the features.<sup>11</sup>

In contrast, factors that were most correlated with daytime SUID included older infants, day care, white infants, sleeping in an adult bed, put to sleep in prone position, found in prone position, death not related to sleep environment, sleeping on the floor and other places of death (Table 1).

Bed sharing is the strongest variable associated with nighttime SUID and explains part of the age difference between nighttime and daytime SUID. However, even after restricting our analysis to non-bed sharing infants only, we see very similar statistical results. 10:00-21:00 and 22:00-09:00 continue to be highly statistically differentiable, and the variables for nighttime or daytime death remain very similar, with older infants, day care and sleeping in an adult bed being most correlated with daytime SUID (data not shown).

Several features were not associated with time of death including maternal smoking, sex of infant, breastfeeding and caregiver's income.

### 4 | DISCUSSION

Consistent with previous reports, the majority of SUID cases occur during nighttime sleep. A common reported scenario is that an apparent healthy infant is placed to sleep in the evening and found dead in the morning. Thus, the exact time of death is unknown, and this is indeed likely for most cases found around the time when the parents wake up. At the younger ages (0-2 months), at which the risk is especially high for a nighttime death, babies are generally sleeping in short stretches due to needing to be fed and changed regularly, the anticipation of frequent waking increases the chance of finding the infant within a shorter interval of actual death. In this study, there are deaths reported at all hours from the late evening to morning with a clear pattern of progressively increasing number of SUID cases discovered each hour between 00:00 and 07:00 (Figure 1). In addition, the statistically determined day and nighttime time

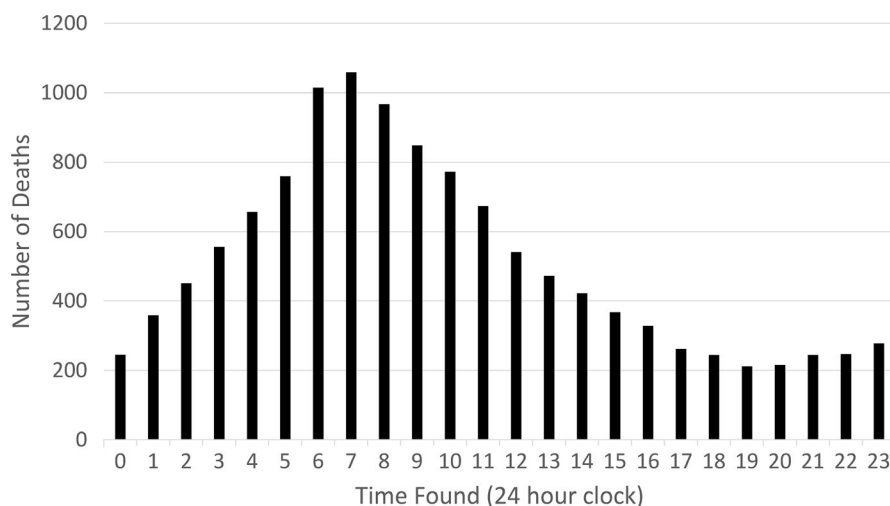


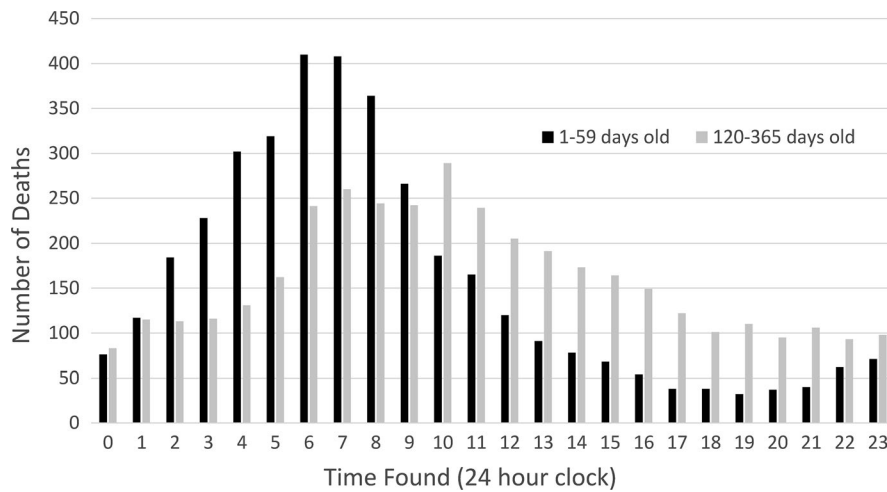
FIGURE 1 Distribution of time of death

**TABLE 1** Prevalence of risk factors that were significant and unadjusted and adjusted odds (OR) ratios and their 95% confidence intervals (CI)

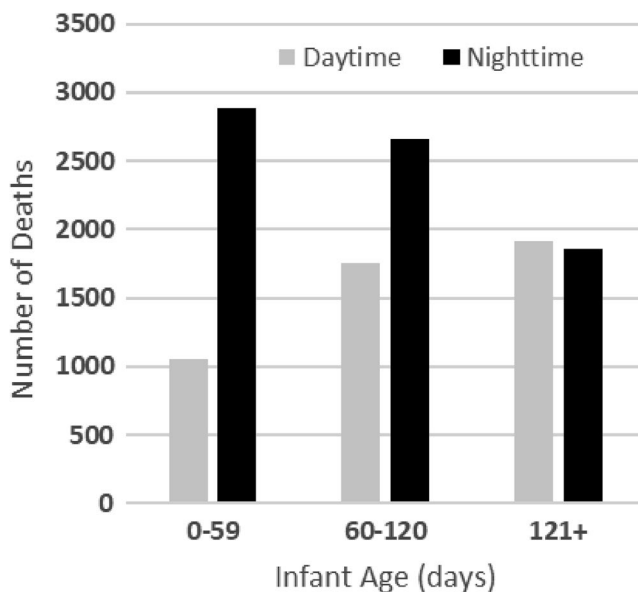
	Daytime N (%)	Nighttime N (%)	OR (95% CI)	AOR (95% CI)
<b>Infant age</b>				
0-59 days	1052 (22.3%)	2891 (39.1%)	0.45 (0.41, 0.49)	0.56 (0.51, 0.61)
60-120 days	1754 (37.2%)	2656 (35.9%)	1.06 (0.98, 1.14)	0.99 (0.91, 1.07)
121+ days	1914 (40.6%)	1854 (25.1%)	2.04 (1.88, 2.20)	1.72 (1.58, 1.88)
<b>Race</b>				
White	3050 (64.5%)	4084 (55.1%)	1.48 (1.37, 1.59)	1.34 (1.22, 1.46)
Non-white	1681 (36.5%)	3329 (44.9%)	0.68 (0.63, 0.73)	0.75 (0.68, 0.82)
<b>Primary caregiver</b>				
Parent	4368 (92.3%)	6973 (94.1%)	0.76 (0.66, 0.88)	0.83 (0.69, 0.99)
Not parent	363 (7.7%)	440 (5.9%)	1.32 (1.14, 1.52)	1.21 (1.01, 1.45)
<b>Death related to sleep environment</b>				
Yes	4241 (89.7%)	7078 (95.5%)	0.41 (0.35, 0.47)	0.49 (0.33, 0.72)
No	490 (10.3%)	335 (4.5%)	2.44 (2.11, 2.82)	2.05 (1.39, 3.00)
<b>Other place of death</b>				
Yes	213 (4.5%)	222 (3.0%)	1.53 (1.26, 1.85)	1.57 (1.27, 1.94)
No	4518 (95.5%)	7191 (97.0%)	0.65 (0.54, 0.79)	0.64 (0.52, 0.79)
<b>Day care</b>				
Yes	460 (9.7%)	51 (0.7%)	15.55 (11.6, 20.8)	8.79 (6.48, 11.9)
No	4271 (90.3%)	7362 (99.3%)	0.06 (0.05, 0.09)	0.11 (0.08, 0.15)
<b>In adult bed</b>				
Yes	1685 (35.6%)	3693 (49.8%)	0.56 (0.52, 0.60)	2.15 (1.11, 4.19)
No	3046 (64.4%)	3720 (50.2%)	1.79 (1.67, 1.93)	0.46 (0.24, 0.90)
<b>Bed sharing</b>				
Yes	1401 (29.6%)	4593 (62.0%)	0.26 (0.24, 0.28)	0.28 (0.25, 0.31)
No	3330 (70.4%)	2820 (38.0%)	3.87 (3.58, 4.19)	3.57 (3.18, 4.02)
<b>Sleeping on floor</b>				
Yes	72 (1.5%)	100 (1.3%)	1.13 (0.83, 1.53)	2.18 (1.04, 4.60)
No	4659 (98.5%)	7313 (98.7%)	0.88 (0.65, 1.20)	0.46 (0.22, 0.96)
<b>Position placed to sleep</b>				
Stomach	1045 (22.1%)	1272 (17.2%)	1.37 (1.25, 1.50)	1.27 (1.12, 1.45)
Back	1598 (33.8%)	2918 (39.4%)	0.79 (0.73, 0.85)	0.81 (0.71, 0.92)
Side	496 (10.5%)	845 (11.4%)	0.91 (0.81, 1.02)	1.05 (0.90, 1.22)
Unknown	1592 (33.7%)	2378 (32.1%)	1.07 (0.99, 1.16)	0.86 (0.71, 1.04)
<b>Position found</b>				
Stomach	1851 (39.1%)	2238 (30.2%)	1.49 (1.38, 1.60)	1.28 (1.13, 1.45)
Back	877 (18.5%)	1987 (26.8%)	0.62 (0.57, 0.68)	0.76 (0.66, 0.86)
Side	438 (9.3%)	895 (12.1%)	0.74 (0.66, 0.84)	1.05 (0.90, 1.23)
Unknown	1565 (33.1%)	2293 (30.9%)	1.10 (1.02, 1.19)	1.07 (0.87, 1.31)

divisions make sense since the vast majority of nighttime deaths would be discovered before 09:00. Together, these factors lend credence to the general overall pattern of time of death reported here, despite the limitation that time of discovery is used as time

of death. Not knowing the exact time of death is the norm when it comes to SUID, and previous case-control studies have attempted to estimate time of death, such as using the midpoint between time last seen alive and time found dead. However, this technique will



**FIGURE 2** Distribution of time of death for infants aged 0-59 days and 120+ days of age



**FIGURE 3** Distribution of time of death categorised as daytime and nighttime and infant age categorised as 0-59, 60-120 and 121+ days of age

produce measurement error, especially for nighttime sleep, as the interval between last seen alive and found dead will, in general, be greater. We acknowledge that using time found dead is also imprecise; however, using advanced statistical methods, time of death was subsequently dichotomised to day or night time, and thus, measurement error would only be likely for cases at around the cut-points (09:00-10:00 and 21:00-22:00).

Perhaps the biggest strength of this study is the large population size. Most studies analysing time of death in association with sudden infant death have been limited to several hundred cases in contrast to the >12 000 SUID cases reported here. We were thus able to bring much higher granularity to the comparative analysis of risk factors between the nighttime and daytime sleep environments. Another strength is the advanced statistical modelling techniques used in the analysis.

There were differences between those with time of death recorded (60.9%) and those without (39.1%). In most instances, the

differences were small; for example, the mean age of caregiver where time found was recorded was 25.7 years versus 25.4 years for those without time recorded. However, cases with a reported time of death were much less likely to be bed sharing than those without a recorded time of death (63% vs. 72%,  $p < 0.05$ ). Missing data, especially for the time found, may produce selection bias. A further limitation is that this is not a population-based study. The data source does not include every SUID case nationwide and, therefore, may not be representative of all SUID cases and cannot be compared directly with vital statistics data.<sup>13</sup>

Much of our findings agreed with previous accounts including bed sharing correlating with nighttime deaths and prone sleep position correlating with daytime deaths. However, there were some key differences in our data compared to previous studies. The correlation between nighttime deaths and younger infants had been previously reported, but was thought to be explained by bed sharing.<sup>14,15</sup> However, we found that even after controlling for bed sharing, younger infants were still at higher risk during the nighttime hours. In addition, controlling for day-care attendance, older infants remain at a higher risk during the day. This is biologically interesting, since the sleep patterns of younger versus older infants differ markedly. Younger infants spend 50% of the total sleep time in REM sleep, while infants aged 8 or 9 months spend 20%-25% in REM.<sup>16</sup> REM sleep is considered a state of autonomic instability,<sup>17,18</sup> and neurons involved in the control of REM sleep are tightly linked to arousal networks and autonomic control.<sup>19</sup> Thus, a vulnerable child is more likely to succumb to SUID during REM sleep if these mechanisms are disturbed. Moreover, the proportion of REM sleep increases later in sleep, which includes the early morning hours.<sup>20</sup>

Even restricting to only those infants who were at home and not bed sharing at the time of death, we still observe two separate distribution patterns that peak in the early morning hours for younger infants and during the daytime for older infants (Figure S1).

Maternal cigarette smoking is strongly associated with SUID,<sup>21</sup> and it has been argued that the association is causal.<sup>22</sup> Maternal cigarette smoking has been cited in association with nighttime infant SIDS deaths in several studies.<sup>2,4,6</sup> In our study, however, there was

no association between maternal cigarette smoking and nighttime death after adjusting for the other features in our data set. This is true for smoking before and during pregnancy and for second-hand smoke exposure.

In addition to smoking, other features that were also not associated with time of death after controlling for the full feature set included, sex of infant, breastfeeding and caregiver's income and age. These observations suggest that the diurnal variation in SUID risk is not related to socioeconomic status.

This is one of the first studies to report a racial difference in time of death (aside from a reported increased risk of nighttime death in the Maori population<sup>2</sup>). This is likely due to the fact that the United States has a more racially heterogeneous population compared to other countries that have analysed similar data. We found that non-white infants correlated with nighttime deaths, while white infants were associated with daytime deaths. This could in part be explained by the fact that bed sharing is more common among black infants compared to other races.<sup>23,24</sup>

Similar to the New Zealand<sup>2</sup> and Nordic<sup>4</sup> studies, prone sleep position was found to be associated with daytime deaths. Mitchell and Williams speculate that prone sleeping is equally risky regardless of the time of day and that a separate risk factor that is specific to the nighttime reduces the magnitude of risk from prone sleeping at night.<sup>25</sup> Whether or not this is true, the observation underscores the importance of educating parents and non-parental caregivers (inside and outside the home) that placing an infant to sleep in a supine position is just as important during daytime naps as for nighttime sleep. The message distils down to 'Make every sleep a safe sleep'.<sup>26</sup>

After controlling for all features in the dataset, the factors that are associated with the greatest risk of a nighttime SUID death includes bed sharing, young infants, non-white infants and supine sleep position. In contrast, factors associated with daytime SUID included older infants, day-care attendance, white infants and prone sleep position. The circadian variations in SUID risk factors described here suggest different underlying causal mechanisms of death, and these data should provide clues towards future physiological and genetic research dedicated to uncovering the mechanistic differences.

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#### CONFLICT 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.

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