Sudden Infant Death Syndrome and Residential Altitude

David Katz, MDa, Supriya Shore, MDb, Brian Bandle, MPHc, Susan Niermeyer, MD, MPHd, Kirk A. Bol, MSPHe, Amber Khanna, MDa

abstract

BACKGROUND: Theories of sudden infant death syndrome (SIDS) suggest hypoxia is a common pathway. Infants living at altitude have evidence of hypoxia; however, the association between SIDS incidence and infant residential altitude has not been well studied.

METHODS: We performed a retrospective cohort study by using data from the Colorado birth and death registries from 2007 to 2012. Infant residential altitude was determined by geocoding maternal residential address. Logistic regression was used to determine adjusted association between residential altitude and SIDS. We evaluated the impact of the Back to Sleep campaign across various altitudes in an extended cohort from 1990 to 2012 to assess for interaction between sleep position and altitude.

RESULTS: A total of 393,216 infants born between 2007 and 2012 were included in the primary cohort (51.4% boys; mean birth weight 3194 ± 558 g). Overall, 79.6% infants resided at altitude <6000 feet, 18.5% at 6000 to 8000 feet, and 1.9% at >8000 feet. There were no meaningful differences in maternal characteristics across altitude groups. Compared with residence <6000 feet, residence at high altitude (>8000 feet), was associated with an adjusted increased risk of SIDS (odds ratio 2.30; 95% confidence interval 1.01–5.24). Before the Back to Sleep campaign, the incidence of SIDS in Colorado was 1.99/1000 live births and dropped to 0.57/1000 live births after its implementation. The Back to Sleep campaign had similar effect across different altitudes (P = .45).

CONCLUSIONS: Residence at high altitude was significantly associated with an increased adjusted risk for SIDS. Impact of the Back to Sleep campaign was similar across various altitudes.

WHAT'S KNOWN ON THIS SUBJECT: Various clinical and demographic factors are associated with sudden infant death syndrome (SIDS), and an association between altitude of residence and SIDS has been questioned but not yet demonstrated in any large observational studies.

WHAT THIS STUDY ADDS: This study demonstrates an association between altitude and SIDS, with higher SIDS rates observed at high elevation (>8000 feet) than at the more moderate elevations (<6000 feet).
Sudden infant death syndrome (SIDS) involves the tragic, unexplained death of an infant. Historically, SIDS accounted for a significant percentage of infant deaths with an incidence of 1.2/1000 live births in the 1990s. The incidence declined to 0.43/1000 live births in the United States by 2011, likely because of public health campaigns. SIDS remains the third leading cause of infant mortality, accounting for 7.2% of total infant deaths. Although maternal smoking, low socioeconomic status (SES), and prone sleeping position have been strongly associated with SIDS, small clinical studies have implicated hypoxia as a potentiating factor, but causality has not been established. Two case-control studies have demonstrated an association between increasing altitude and SIDS. A study from Nebraska in the 1970s reported data from a peak elevation of 4740 feet, and a study from Austria included infants residing at higher altitudes and found prone sleeping position to be an “obligatory cofactor” for the observed association between SIDS and altitude. A small death certificate study in Colorado from 1975 to 1978 compared infants who died of SIDS with infants who died of other causes and found no association with altitude but included few SIDS events and performed limited analysis.

In the United States, the well-known Back to Sleep campaign began to promote supine sleeping for SIDS prevention in 1994. This public health campaign is credited with an ~50% reduction in the rate of SIDS in the United States. Although SIDS rates are also down globally, they have stabilized and there has been a call for action to further reduce the risk. The relationship between SIDS and altitude has not been evaluated in the Back to Sleep era with more robust birth certificate data. It is also unknown if the impact of this campaign has been uniform across all altitudes in Colorado. A disproportionate reduction in SIDS at high altitude would support the interaction between prone sleeping and SIDS at altitude observed in the aforementioned Austrian study.

By using the large, multiyear Colorado linked birth certificate and infant death registries, we sought to assess the relationship between altitude and SIDS in Colorado and the effect of the Back to Sleep campaign on the incidence of SIDS both statewide and by altitude of residence. We hypothesized that the incidence of SIDS is greater at higher altitudes and that this finding was not affected by the Back to Sleep campaign.

METHODS
Data Source and Study Design
We conducted a retrospective cohort study by using Colorado birth certificate and infant death registries data over a 22-year period (1990–2012) provided by the Colorado Department of Public Health and Environment (CDPHE). Birth data were available in the form of 2 data sets: 1 data set for births from 1990 to 2006 and 1 data set for births from 2007 to 2012. CDPHE implemented the 2003 Revision of the US Standard Certificate of Live Birth, beginning with 2007 births, resulting in differences in some data elements, including race/ethnicity, maternal education, and marital status. Other differences include an increase in the number of available covariates in the latter data set.

The primary analysis was performed by using the more expansive 2007 to 2012 data set to characterize the association between altitude and SIDS in the modern, post–Back to Sleep era. A secondary analysis was performed by using data from 1990 to 2012 to assess the impact of the Back to Sleep campaign and assess for differing effects of the campaign at different altitudes.

Infant mortality data were linked to birth data by CDPHE. Altitude of maternal residence at time of birth was geocoded by using residence addresses reported on the birth certificate, and subsequently released by CDPHE in increments of 500 feet to preclude registrant identification. This study was deemed not to constitute human subjects research, as the data are publicly available, de-identified, and did not involve investigator contact with study subjects.

Study Population and Setting
The study population included all infants born in Colorado, to mothers residing in Colorado, from 1990 to 2012. We excluded infants with documented congenital abnormalities as defined according to the 2003 revision of the US Standard Certificate of Live Birth. To create distinct pre- and post–Back to Sleep periods, we excluded infants born during the implementation period of the Back to Sleep campaign (1994–1996).

Measures
Outcome Variable
The primary dichotomous outcome measure used for both analyses was the occurrence of SIDS. Identification of SIDS was based on International Classification of Disease, Ninth Revision code of 789.0 for deaths before 1999 or a 10th Revision code of R95 for deaths during or after 1999.

Exposure Variables
Residential altitude was the primary exposure variable for the analysis examining association between residential altitude and SIDS. For this analysis, residential altitude was categorized into 3 comparison groups: front range (<6000 feet), lower mountain (6000–8000 feet), and upper mountain (>8000 feet). There are not standard altitude categories in the literature. These ranges were chosen a priori to allow all of the Denver metropolitan area to be in 1 category (<6000 feet) and to have sufficient population in the highest altitude group.

A dichotomous variable indicating if an infant’s birth took place before or after
the implementation of the Back to Sleep campaign was used as the exposure variable of interest for the secondary analysis. Infants born between 1990 and 1993 were categorized as pre–Back to Sleep births. Infants born after January 1, 1997, were considered post–Back to Sleep births. Infants born between 1994 and 1996 were considered to have been born during the program implementation phase of Back to Sleep and were excluded from the analysis. The significance of interaction between altitude and birth in the pre– versus post–Back to Sleep era was tested.

Covariates
Potential confounders for the association between residential altitude and SIDS were included based on clinical rationale and/or previous studies. These covariates included infant factors (infant gender; birth weight; breastfeeding at time of discharge; birth injury); maternal factors (age; race; education; alcohol consumption; cigarette smoking; Women, Infants, and Children [WIC] program participation; number of prenatal care visits; and pregnancy risk factors) and paternal factors (age, race, and education). Maternal education and WIC program participation were used as markers for SES.18,19 WIC participation requires household income <185% of the federal poverty line.20 Missing values for categorical variables were categorized into an “unknown” group for comparison.

The limited covariates available for the secondary analysis included infant gender, birth weight, maternal age, race, education, marital status, smoking status, number of terminated pregnancies (including spontaneous or induced losses or ectopic pregnancies), number of previous births, altitude of residence, and paternal age, race, and education.

Statistical Analysis
Distributions of the characteristics of interest for births were calculated for the total 2007 to 2012 cohort for the primary model and the pre– and post–Back to Sleep cohorts for the secondary analysis. One way of variance was used for comparisons of continuous variables and chi-squared tests were used for comparisons of categorical variables.

We used a purposeful selection approach to develop both logistic regression models.21,22 Variables with a univariate analysis $P \leq .25$ were selected as candidates for inclusion in the multivariate analysis. These variables were then tested for significance ($P < .05$), and also tested for effect modification and confounding. Variables that were both not significant and not confounders were removed from the model, and then added back into the model one at a time testing only these variables for significance and confounding.

A Hosmer-Lemeshow statistic was produced for each final regression model to examine the stability of the modeled estimates. A nonsignificant chi-squared statistic ($P > .05$) was used to indicate that the final model was an appropriate fit.

RESULTS
Baseline Characteristics
Between January 1, 2007, and December 31, 2012, a total of 404,270 infants without congenital anomalies noted at birth were born to mothers residing in Colorado. A total of 11,054 (2.7%) infants were categorized as “unknown altitude” because of lack of data on residential altitude and the final cohort was composed of 393,216 infants. Supplemental Table 3 shows characteristics of patients without data on residential altitude compared with those with data on residential altitude. There were no clinically meaningful differences between those with and without a known elevation.

Overall, 202,113 (51.4%) infants were boys, and the mean birth weight of the study population was 3,194 ± 558 g. Most of the cohort resided at an altitude of <6,000 feet ($n = 312,919$; 79.6%), with fewer residing at 6,000 to 8,000 feet ($n = 72,672$; 18.5%) and fewer still at >8,000 feet ($n = 76,251$; 1.9%). Table 1 shows baseline characteristics of the study cohort. There were no meaningful differences between maternal or infant characteristics across various altitudes. The statistically significant differences found for some variables are likely a result of the large cohort size.

Association Between Residential Altitude and SIDS Incidence
The overall incidence of SIDS between 2007 and 2012 was 0.42/1,000 live births. In 2012, the last year included in the study, the rate of SIDS was 0.20/1,000 live births in Colorado. Figure 1 shows SIDS incidence stratified by residential altitude in the cohort. The incidence was lowest among infants residing at <6,000 feet, increasing progressively with increasing altitude. Figure 2 demonstrates the distribution of SIDS and possible SIDS-related diagnosis codes by altitude category. Table 2 shows results of the logistic regression model examining adjusted association between residential altitude and SIDS.

Compared with infants residing at an altitude of <6,000 feet, there was no increase in odds for SIDS among those residing between 6,000 and 8,000 feet (odds ratio [OR] 1.29, 95% confidence interval [CI] 1.01–1.52). Other variables that were statistically significantly associated with SIDS in this model were black paternal race (OR 2.05, 95% CI 1.06–3.97), higher number of previous live births (OR 1.21, 95% CI 1.08–1.34), smoking during pregnancy (OR 2.69, 95% CI 1.85–3.91), presence of birth injuries (OR 1.52, 95% CI 1.03–2.22) and lower birth weight (OR 1.05 per 100-g decrease, 95% CI 1.01–1.07).
Paternal race was associated with SIDS. Paternal and maternal race were highly concordant (r = 0.89), raising the possibility of confounding due to colinearity. However, when paternal race was excluded from our model, we did not find a significant association between paternal race and SIDS in our multivariable model (OR 1.02, 95% CI 0.5–2.08 for “black” and OR 0.82, CI 0.41–1.64 for “other” race).

Measures of SES were considered in the model, including participation in a WIC program, and maternal educational status. Measures of these variables were numerically similar across elevation strata. Although WIC participation was associated with SIDS in univariate analysis (OR 1.63, 95% CI 1.18–2.24), it was not statistically significantly associated with SIDS after adjustment for covariates (OR 1.20, 95% CI 0.82–1.75) and was not included in the final model. Increasing levels of maternal education was associated with decreased risk of SIDS in multivariable analysis (OR 0.87, 95% CI 0.78–0.96 per 1 level of increase in maternal education).

### Impact of the Back to Sleep Campaign Across Altitudes

In the expanded cohort that included infants born between 1990 and 2012, we observed a significant decrease in SIDS incidence from 1.99/1000 live births in the pre–Back to Sleep (1990–1993) era to 0.57/1000 live births in the post–Back to Sleep era.
births in the post–Back to Sleep era (1997–2012) \( (P \leq .001 \text{ for the trend}) \). During this same time period, overall infant mortality decreased significantly and proportionally (Fig 3). There was no significant association among SIDS, residential altitude, and birth in the pre–versus post–Back to Sleep era \( (P = .45) \), suggesting that the impact of the Back to Sleep campaign has been similar across all altitudes in Colorado.

**DISCUSSION**

This study demonstrates that altitude of residence is independently associated with an increased incidence of SIDS, specifically among infants born to mothers living at >8000 feet of altitude. We found no evidence that the Back to Sleep campaign caused a disproportionate drop in SIDS incidence at higher altitudes. This finding suggests prone sleeping is not a requisite for SIDS at altitude.

Our findings are consistent with 2 previous case-control studies, although the altitudes in our study are much higher than either of them.\textsuperscript{13,14} Our study confirms that even in the modern era, with strong public health information promoting healthy sleep habits, high altitude remains associated with SIDS.

Although a previous, smaller, study from Colorado did not find an altitude effect, it compared SIDS deaths with non-SIDs deaths above and below 7500 feet. The authors were unable to determine the number of infants living at higher altitudes and unable to control for any other factors associated with SIDS.\textsuperscript{15}

It has been suggested that hypoxia may contribute to the pathophysiology of SIDS. Modifiable factors, such as prone sleeping and tobacco exposure, facilitate hypoxia and the resultant decreased cerebral oxygenation may play a mechanistic role in SIDS. Living at high altitude also is associated with decreased oxygenation,\textsuperscript{23} and it therefore may be that a greater incidence of hypoxia is responsible for the greater incidence of SIDS at high altitude. However, further investigation is required to understand the relationship. Additionally, it remains unclear if altitude has a linear or threshold effect. Based on the previous studies, which found an altitude effect at lower altitudes than in our study, it is possible that the incidence of SIDS increases linearly with increasing altitude.

Although relatively few people reside at high altitude in the United States, globally, 63 million people live above 8000 feet.\textsuperscript{24} Previous work has shown that infants born and raised at high altitudes are at risk for lower birth weight, symptomatic high-altitude pulmonary hypertension, and persistence of fetal vascular connections.\textsuperscript{25} Countries with large populations living at altitude include Bolivia, Colombia, Peru, Bhutan, Kazakhstan, Nepal, Tajikistan, and Ethiopia. Studies on the risk of SIDS in countries with a high proportion of people living at high altitude would be limited by access to medical care, SES, genetic adaption to altitude, and death scene investigation necessary to diagnose SIDS. Despite these limitations, a better understanding of chronic hypoxia and a potential link to SIDS may lead to improved

![FIGURE 1](image_url)

**FIGURE 1**

SIDS incidence per 1000 live births stratified by residential altitude. Incidence per 1000 live births (95% Wald Confidence Limits).

![FIGURE 2](image_url)

**FIGURE 2**

Incidence of SIDs, accidental suffocation, and death of unknown cause per 1000 live births stratified by residential altitude. Incidence per 1000 live births (95% Wald Confidence Limits): <6000 feet: SIDS 0.40 (0.34–0.48); unknown 0.19 (0.15–0.24); accidental suffocation 0.11 (0.08–0.16). 6000–8000 feet: SIDS 0.45 (0.32–0.64); unknown 0.17 (0.09–0.29); accidental suffocation 0.12 (0.06–0.24). >8000 feet: SIDS 0.79 (0.35–1.75); unknown 0.13 (0.02–0.93); accidental suffocation 0.13 (0.02–0.93).
recommendations and targeted interventions for these populations.

As previous studies have documented, the Back to Sleep campaign has been very successful at reducing the rate of SIDS.\textsuperscript{1} This study corroborated the results of other large cohort studies with infants in the post–Back to Sleep era having a decreased risk of SIDS (OR 0.295, 95% CI 0.26–2.64).\textsuperscript{26–28} The concomitant decrease in overall infant mortality suggests that the observed decrease in SIDS incidence is not a function of changing definition or better investigation of infant deaths over time. There remains strong evidence to encourage parents to place infants on their back every time they sleep. This study also confirmed several factors that have been previously associated with SIDS. Smoking, decreased birth weight, and lower SES status were associated with increased risk of SIDS.\textsuperscript{3–10} Other studies that have linked birth certificate registry data with infant mortality registry data have found similar trends in parity and birth weight.\textsuperscript{29,30} Paternal race and birth injury were associated with SIDS in this study, which have not been documented in previous work. It is not clear if these variables were included in other models of SIDS. The findings suggest future work is needed to fully evaluate the risk of SIDS.

It is important to note that the current risk of SIDS is lower than it was historically, occurring in 0.42/1000 live births in Colorado between 2007 and 2012. Even though the odds of SIDS are greater at altitudes above 8000 feet, the absolute incidence of SIDS at altitudes above 8000 feet remains low at 0.79/1000 live births. Although our findings do not support abandonment of high-altitude residences, they do highlight the importance of further investigation into the pathophysiology of SIDS at high altitude.

This study is subject to the limitations of observational research, including unmeasured confounding and missing data. In particular, fewer detailed data collection on the birth certificate form used until 2007 limits multivariate assessment of potential confounders during the pre– and early post–Back to Sleep years. More detailed data from 2007 to 2012, however, allow description of the factors relevant to understanding SIDS in the modern era.

Altitudes in this study were those of maternal residence at the time of infant birth and therefore may not represent infant altitude at the time of death. This study is also limited in the range of altitudes assessed. We cannot describe the association of SIDS with altitudes more extreme than those studied here, nor can we assess whether the moderate altitudes inhabited by our reference group are associated with a higher incidence of SIDS relative to sea level.
SES has been noted to be a strong predictor of SIDS risk. This study used WIC participation and maternal education as markers of SES, although other markers of SES exist; hence, SES may still confound the results of this study. Other potential confounders, such as hematocrit, were not available in the dataset.

Finally, all deaths coded as SIDS were assumed to be correct. SIDS is a diagnosis of exclusion which is dependent on death scene investigation, for which national standards have been set. It has been suggested that not all SIDS-coded deaths may be accurate. Case files were not available for review, and inspection audits were not performed for this study. Coroners in Colorado are employed by counties, making geographic and temporal variability in infant death investigation possible. Household and certain environmental factors, such as local weather around the time of the SIDS event, are not captured in this administrative data, and therefore could not be assessed.

**REFERENCES**


**CONCLUSIONS**

As has been demonstrated for the country as a whole, the Back to Sleep campaign significantly reduced the incidence of SIDS in Colorado. Importantly, although the overall risk of SIDS is now low, these data suggest that altitude is independently associated with SIDS. This finding should be considered when counseling expectant families and new parents, and requires further investigation to demonstrate the pathophysiology behind the observed association.

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