Prematurity and Sudden Unexpected Infant Deaths in the United States

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abstract

BACKGROUND AND OBJECTIVES: Prematurity, a strong risk factor for sudden unexpected infant death (SUID), was addressed in recommendations by the American Academy of Pediatrics in 2011 for safe sleep education in NICUs. We documented associations between gestational age (GA) and SUID subsequent to these guidelines.

METHODS: Using the 2012–2013 US linked infant birth and death certificate period files, we documented rates per live births of sudden infant death syndrome, ill-defined and unspecified causes, accidental suffocation and strangulation in bed, and overall SUID by GA in postneonatal, out-of-hospital, and autopsied cases; compared survivors and cases; and estimated logistic regression models of associations between GA and SUID.

RESULTS: SUID cases were more likely than survivors to be <37 weeks' GA (22.61% vs 10.79%; $P < .0001$). SUID rates were 2.68, 1.94, 1.46, 1.16, 0.73, and 0.51 per 1000 live births for 24 to 27, 28 to 31, 32 to 33, 34 to 36, 37 to 38, and 39 to 42 weeks' GA, respectively. Logistic regression models additionally indicated declines in the risk for SUID as GA increased. Prenatal smoking, inadequate prenatal care, and demographics associated with poverty were strongly associated with SUID.

CONCLUSIONS: Despite the 2011 American Academy of Pediatrics recommendations for increased safe sleep education in the NICUs, SUID rates were inversely associated with GA in 2012 to 2013, suggesting that risk of SUID associated with prematurity has multiple etiologies requiring continued investigation, including biological vulnerabilities and the efficacy of NICU education programs, and that strategies to reduce SUID should be multifaceted.

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WHAT'S KNOWN ON THIS SUBJECT: Recognizing that prematurity is a major risk factor for sudden unexpected infant death, the American Academy of Pediatrics enhanced its recommendations for providing safe infant sleep education to parents of infants in NICUs in 2011.

WHAT THIS STUDY ADDS: The inverse relationship between sudden unexpected infant death rates and gestational age despite the American Academy of Pediatrics recommendations for safe sleep education in NICUs, calls for additional examination of intrinsic risk factors and the efficacy of education programs.

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The rate of sudden infant death syndrome (SIDS) in the United States declined from 1.20 per 1000 live births in 1992, the year the American Academy of Pediatrics (AAP) first issued its recommendation for supine sleep, to 0.51 in 2010, the year preceding its 2011 recommendations addressing SIDS and other sleep-related infant deaths.[1,2] Declines occurred across all gestational age (GA) groups, with 44.8%, 25.8%, 20.0%, 19.6%, and 30.8% reductions in rates for infants with GAs of 28 to 31, 32 to 33, 34 to 36, 37 to 38, and 39 to 40 weeks, respectively, between 1999 and 2010.[2,3] However, SIDS remained inversely associated with GA; for example, the rate in 2010 was 1.39 per 1000 for infants born at 28 to 31 weeks compared with 0.36 for term infants. The elevated risk associated with younger GA has been attributed to physiologic, social, and environmental factors.[4,5] For example, some studies have found that preterm infants are more likely to be placed prone and to bed-share, which are major risk factors for SIDS,[6,7] and that the combination of prematurity and environmental conditions multiplies the risk.[8]

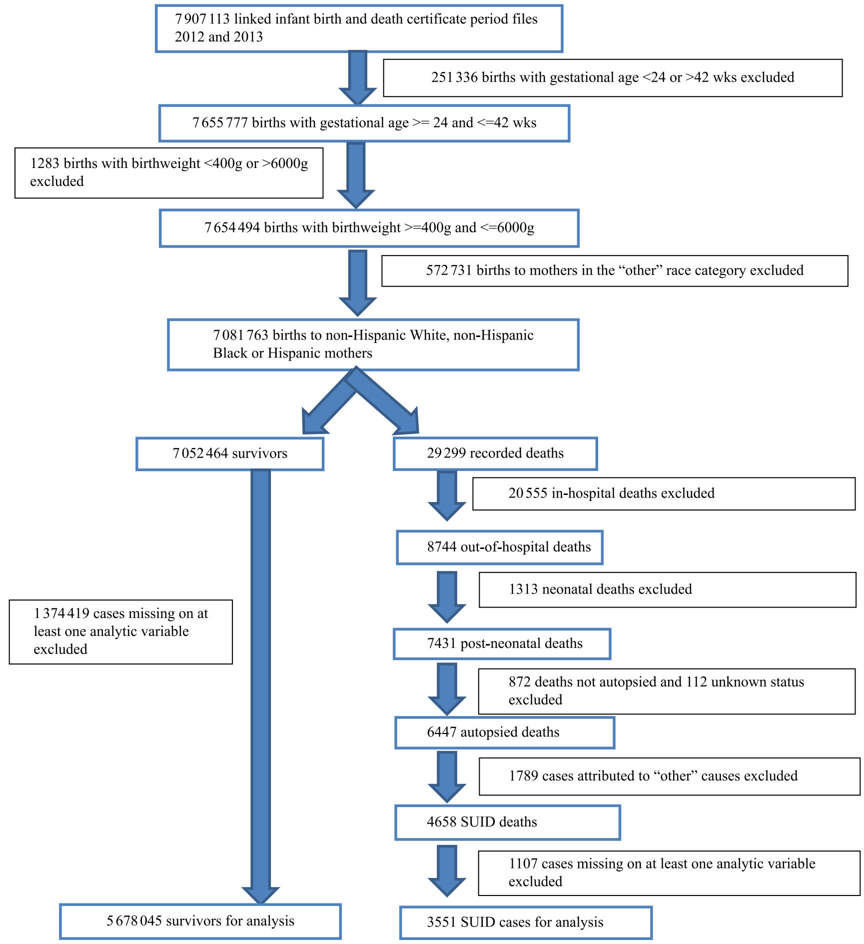

FIGURE 1
Sample inclusion/exclusion flowchart.

Along with SIDS, other sleep-related infant deaths categorized as ill-defined and unspecified causes of mortality (IUCM) and accidental suffocation and strangulation in bed (ASSB) comprise a broad category termed sudden unexpected infant deaths (SUID).[4,9] Variations in the application of these diagnoses have generated a diagnostic shift, which is reflected in a decline in SIDS alongside an increase in other sleep-related deaths, making it important to consider the full grouping of SUID.[9] Similarities in risk factors across causes have also led to the inclusion of the broader grouping in research studies.[4,10] SUID is now among the health indicators tracked for Healthy People 2020.[9,10]

We sought to determine the association between GA and SUID in US births subsequent to the 2011 Safe Infant Sleep Guidelines of the AAP, which provided recommendations to help NICUs educate parents, model safe sleep guidelines, and develop supportive policies.[4]

METHODS

Linked US infant birth and death certificate period files for 2012 and 2013 were downloaded from the National Center for Health Statistics Web site.[11] Data for the 7 907 113 births from this period were pooled. The sample was limited to births with GAs of 24 to 42 completed weeks and birth weights of 400 to 6000 g, reducing the births for analysis to 7 654 494. Exclusion of births to mothers in an “other” race category additionally reduced the sample to 7 081 763. Of the 29 299 recorded deaths in this sample, 46.4% were postneonatal (>27 days of age); 29.8% were outside of a hospital; and 43.2% received autopsies. Of the 6447 deaths that met all conditions (postneonatal, outside of a hospital, and autopsied), 1789 were attributed to causes other than SUID and excluded, additionally reducing available cases to 7 057 122 births consisting of 7 052 464 survivors and 4658 SUID-attributed deaths. Figure 1 presents an inclusion/exclusion flowchart.

SUIDs were defined based on *International Classification of Diseases*, *Tenth Revision* (ICD-10) codes as R95 (SIDS), R99 (IUCM), and W75 (ASSB) in keeping with the criteria for Healthy People 2020. GA was categorized as 24 to 27, 28 to 31, 32 to 33, 34 to 36, 37 to 38, and 39 to 42 weeks.[2]

The analysis included maternal demographic, obstetric, and behavioral characteristics commonly associated with SIDS and other sleep-related infant deaths. Demographic characteristics included race/ethnicity, marital status, age, and education. Obstetric characteristics included gravida, delivery mode, sex, and multiple birth. Behavioral characteristics included prenatal cigarette smoking and prenatal care use measured by the Adequacy of Prenatal Care Utilization (APNCU) Index, addressing both the timing of care initiation and the number of visits compared with what is recommended for an infant's GA, according to the American College of Obstetrics and Gynecology.[12]

Records with complete information on all analysis variables were used in the main analyses, resulting in an analytic sample of 5 681 596 births (Fig 1). However, in supplementary analyses, we used multiple imputation on a random sample of 20% of the 7 057 122 cases, which allowed us to include cases with missing data on analysis variables other than the outcome and to assess the sensitivity of our estimates.

First, we documented rates per live births of SIDS, IUCM, ASSB, and overall SUID deaths by GA, along with statistical comparisons of death rates between each GA category and full-term births within SUID and each of its subtypes. Next, we compared characteristics of survivors, SUID cases, and SUID subcategories by using χ^2 tests for statistical significance. Then, we estimated logistic regression models of associations between SUID and GA. The first model was unadjusted. The second controlled for demographic and obstetric characteristics. The third added behavioral characteristics. Stata version 13.0 statistical software (Stata Corp, College Station, TX) was used to conduct all analyses. This study met institutional review board standards for exempt review.

TABLE 1 Postneonatal Out-of-Hospital Deaths That Received Autopsy by GA and Cause of Death, United States, 2012 to 2013

GA, wk	Survivors	SIDS (ICD-10: 95)	IUCM (ICD-10: R99)	ASSB (ICD-10: W75)	SUID
24–27	30 096	31 (1.03)[a]	32 (1.06)[a]	18 (0.60)[a]	81 (2.68)[a]
28–31	85 324	90 (1.05)[a]	47 (0.55)[a]	29 (0.34)[a]	166 (1.94)[a]
32–33	107 717	80 (0.74)[a]	44 (0.41)[a]	34 (0.32)[a]	158 (1.46)[a]
34–36	587 500	317 (0.54)[a]	210 (0.36)[a]	158 (0.27)[a]	685 (1.16)[a]
37–38	1 803 062	660 (0.37)[a]	373 (0.21)[a]	288 (0.16)[a]	1321 (0.73)[a]
39–42	4 438 765	1159 (0.26)	562 (0.13)	526 (0.12)	2247 (0.51)

Data not in parentheses are counts; data in parentheses are rates per 1000 live births.
[a] Within cause of death, $P < .000$ for comparison with 39 to 42 weeks' GA by using 2 sample tests comparing proportions.

RESULTS

Of the 7 057 122 births meeting the basic inclusion criteria, 4658 had an out-of-hospital, autopsied, postneonatal death attributed to SUID. Of these, 2337 (50%) were coded as SIDS, 1268 (27%) as IUCM, and 1053 (23%) as ASSB. The overall rate of death from SUID was 0.66 per 1000 live births; the rates for SIDS, IUCM, and ASSB were 0.33, 0.18, and 0.15, respectively (Table 1). For each cause-of-death category and for the combined category of SUID, the rate of death was inversely associated with GA. Within each cause-of-death category, the death rate for each GA category was significantly higher than that for term births ($P < .001$).

The mean postnatal age of death in days was 110.2 for SIDS, 113.0 for IUCM, 112.1 for ASSB, and 111.4 for SUID. Rounded to whole weeks, the corresponding means were 15.7, 16.1, 16.0, and 15.9, respectively. The mean postconceptional age of death, which could be calculated only in whole weeks because GA was available only in weeks, was 53.3 for SIDS, 53.6 for IUCM, 53.8 for ASSB, and 53.6 weeks for the overall SUID category. Postnatal age of death for SUID and its categories decreased and postconceptional age increased with increasing GA (Supplemental Table 4).

Table 2 compares GA and other characteristics of surviving infants with those of SUID cases. In addition to having a higher overall percentage of preterm births compared with survivors (22.6% vs 10.8%), with a nearly fourfold greater difference in the 24- to 27-week GA group, the SUID group had twice the percentage of non-Hispanic African American mothers, 1.7 times the percentage of unmarried mothers, 1.9 times the percentage of mothers <18 years old, 1.7 times the percentage of mothers who had a less than high school–level education, 1.3 times the percentage of mothers with gravida >3, 1.2 times the percentage of boys, 3.9 times the percentage of infants with a birth weight <1000 g, 3.6 times the percentage of mothers who smoked during pregnancy, and 1.7 times the percentage of mothers with inadequate prenatal care (all $P < .001$).

Results from the logistic regression models additionally indicate a decline in the risk for SUID as GA increased (Table 3). In unadjusted and adjusted models, the shortest GA group (24 to 27 weeks) had the highest odds of experiencing SUID (unadjusted odds ratio [OR] = 5.03, 95% confidence interval [CI] = 3.84–6.57; adjusted OR [aOR] = 3.53, 95% CI = 2.69–4.63, model 2). When behavioral factors were added (model 3), the aOR for GA did not change, although there was a strong association between prenatal smoking and SUID (aOR = 2.89, 95% CI = 2.67–3.13) and between both inadequate and intermediate care and SUID (aOR = 1.38, 95% CI = 1.26–1.52 and aOR = 1.31, 95% CI = 1.18–1.46, respectively) (Supplemental Table

5). Maternal race/ethnicity was independently associated with SUID in a pattern widely documented for many birth outcomes.[13] Marital status, age, and education also had strong associations with SUID in the expected directions, as did gravida. Finally, obstetric characteristics (infant sex, multiple birth, and vaginal birth) had independent significant associations in the expected directions with SUID.

Estimates using multiple imputation on a random sample of 20% were similar to those in Table 3 (Supplemental Table 6), suggesting that missing data did not bias the estimates. The estimates were also insensitive to an alternative index of prenatal care (Revised Graduated Index)[12] and to indicators for which trimester prenatal care was initiated instead of an index of prenatal care adequacy (data not shown).

DISCUSSION

We found that postneonatal deaths attributed to SUID and its components were inversely associated with GA in 2012 to 2013.[4] For SUID, SIDS, IUCM, and ASSB, the mortality rates per 1000 live births for postneonatal out-of-hospital deaths were 81%, 75%, 88%, and 80% lower, respectively, for term infants compared with infants with GA in the 24- to 27-week range. In studies on earlier cohorts, the corresponding figures for SIDS were similar at 70% and 73%.[10,14] In logistic regression models, the adjusted odds of SUID were highest for infants with GAs of 24 to 27 weeks, remained so even when risk factors, including smoking and inadequate prenatal care, were controlled for, and uniformly decreased as GA increased, with even the 37- to 38-week group having significantly higher odds of SUID compared with term infants. Our findings are also consistent with previous studies that age of death declined as GA increased.[10]

TABLE 2 Characteristics of Surviving Infants and Infants Who Experienced SUID, United States, 2012 to 2013

	Survivors	SUID	P^a	SIDS (ICD10 95)	IUCM (ICD10 R99)	ASSB (ICD10 W75)	P^b
N	5 678 045	3551		1748	986	817	
GA, wk							
24–27	0.40	1.55	<.000	0.92	2.84	1.35	<.001
28–31	1.15	3.32		3.72	2.94	2.94	
32–33	1.47	3.04		3.03	3.35	2.69	
34–36	8.17	14.70		13.96	16.13	14.57	
37–38	25.56	28.08		27.75	28.90	27.78	
39–42	63.26	49.31		50.63	45.84	50.67	
Mother's race/ethnicity							
Non-Hispanic white	58.61	53.98	<.000	55.89	50.10	54.59	<.001
Non-Hispanic African American	15.10	30.61		28.83	32.05	32.68	
Hispanic	26.28	15.40		15.27	17.85	12.73	
Marital status							
Married	58.69	30.92	<.000	33.81	27.59	28.76	<.001
Unmarried	41.31	69.08		66.19	72.41	71.24	
Mother's age, y							
<18	2.20	4.08	<.000	4.06	4.36	3.79	<.001
18–35	86.74	91.38		91.13	90.77	92.66	
>35	11.06	4.53		4.81	4.87	3.55	
Mother's education							
Less than high school	16.78	28.47	<.000	26.95	30.22	29.62	<.001
High school	25.19	36.95		36.50	38.03	36.60	
More than high school	58.04	34.58		36.56	31.74	33.78	
Gravida							
1	32.40	22.28	<.000	22.43	21.70	22.24	<.001
2–3	39.72	40.58		42.91	38.24	38.43	
>3	27.88	37.14		34.67	40.06	38.92	
Prenatal smoking							
Yes	8.84	32.12	<.000	31.06	30.43	36.47	<.001
No	91.16	67.87		68.94	69.57	63.53	
Prenatal care use (APNCU index)							
Inadequate	13.90	24.08	<.000	22.94	26.06	24.11	<.001
Intermediate	12.04	15.57		15.33	16.84	14.57	
Adequate	38.53	28.56		30.26	25.76	28.27	
Intensive	35.52	31.79		31.46	31.34	33.05	
Vaginal delivery							
Yes	67.36	64.63	<.000	64.24	64.20	65.97	<.005
No	32.64	35.37		35.76	35.80	34.03	
Birth weight, g							
500–999	0.37	1.44	<.000	1.20	2.13	1.10	<.001
1000–1499	0.68	2.37		2.40	2.94	1.59	
1500–2499	6.42	16.09		15.90	17.16	15.20	
≥2500	92.53	80.11		80.49	77.77	82.11	
Girl infant							
Yes	48.84	40.95	<.000	40.73	41.89	40.27	<.001
No	51.16	59.05		59.27	58.11	59.73	
Multiple birth							
Yes	3.38	5.60	<.000	6.01	5.17	5.26	<.001
No	96.62	94.40		93.99	94.83	94.74	

Data are percentages of a given group (survivors, etc) with a given characteristic.

a *P* values from χ^2 tests for significant differences in distributions between survivors and SUID cases.

b *P* values from χ^2 tests for significant differences in distributions across the 3 subtypes of SUID.

Both biological factors and unsafe sleep practices have been suggested as increasing the odds of SUID at lower GAs.[4,15,16] We were unable to explore the role of sleep practices because US death records do not include that information and the Pregnancy Risk Assessment Monitoring System, a surveillance program of the Centers for Disease Control and Prevention (CDC) with information on infant safe sleep practices, is not yet available for 2012 to 2013. Of note, even before the 2011 AAP guidelines, not all studies found that infants with shorter GA were exposed to more adverse sleep practices. In the National Infant Sleep Position Study, there was no significant association between preterm birth (<37 weeks) and supine sleep in 2003 to 2007.[17] Another study using 2000–2011 Pregnancy Risk Assessment Monitoring System data found no less use of the supine position for infants born at <34 weeks' GA compared with term infants.[18] However, this study did find a small positive association when comparing late-preterm to term infants, consistent with findings from an earlier study.[6] Bed-sharing, another risk factor for SUID, was reported to be a usual practice by 11.2% of families in the National Infant Sleep Position Study and was associated with prematurity.[7] However, in a study of hazardous bedding, such as pillows, blankets, and quilts, prematurity was not a significant predictor.[19]

Although there is little suggestive evidence that the observed associations between GA and SUID in 2012 to 2013 were directly related to sleep practices, the pattern could reflect larger effects of adverse sleep practices at younger GAs due to heightened vulnerability of less-developed infants. For example, there is evidence of reduced cerebral oxygenation in the prone position in infants with younger GAs.[8,20] It is also possible that preterm infants experience a greater number of concurrent risk factors, which may have a multiplicative effect. A study of SIDS cases found that 78% had 2 to 7 concurrent risks.[21] In the preterm SIDS cases, 70% were nonsupine at last sleep, over half had mothers and fathers who were smokers, and 43% shared a sleep surface. Future studies should investigate sleep practices and exposure to multiple concurrent risk factors as potential explanations of associations between GA and SUID.

TABLE 3 ORs (95% CIs) for Out-of-Hospital SUID by GA at Birth

	Model 1	Model 2	Model 3
	Unadjusted OR (95% CI)	aOR (95% CI)	aOR (95% CI)
GA, wk			
24–27	5.03*** (3.84–6.57)	3.53*** (2.69–4.63)	3.55*** (2.70–4.66)
28–31	3.71*** (3.08–4.48)	2.71*** (2.24–3.28)	2.73*** (2.25–3.31)
32–33	2.66*** (2.19–3.23)	2.05*** (1.68–2.50)	2.05*** (1.68–2.51)
34–36	2.31*** (2.09–2.55)	1.90*** (1.72–2.11)	1.94*** (1.75–2.15)
37–38	1.41*** (1.30–1.52)	1.30*** (1.20–1.40)	1.34*** (1.23–1.45)
39–42	Ref	Ref	Ref
Observations	5 681 596	5 681 596	5 681 596

Model 1: unadjusted. Model 2: adjusted for maternal race/ethnicity, marital status, age, education, gravidity, infant sex, multiple birth, and vaginal birth. Model 3: adjusted for all characteristics in model 2 plus maternal prenatal smoking and prenatal care use. Full logistic regression results for models 2 and 3 are in Supplemental Table 5. Ref, reference.
*** $P < .001$.

Regardless of whether sleep practices play a role in explaining the observed association between GA and SUID in 2012 to 2013, our findings indicate that enhanced recommendations for safe sleep education in the NICU were not sufficient to reduce or eliminate the inverse association between GA and SUID or its component causes of death. However, we should not infer from our findings that safe sleep guidelines are an ineffective strategy for decreasing the risk of SUID, either overall or as it relates to prematurity. First, rates of SIDS have declined since the guidelines were established, even at young GAs.[1,10] Second, as noted earlier, data on sleep practices by GA are unavailable for the cohort we studied. Third, guidelines can have impact only if they produce behavioral change. Little is known about adherence to safe sleep guidelines after NICU stays and how that might vary by GA, and there is room for improvement in the level of provider knowledge in the NICU, education for parents, and methods used to assess the efficacy of educational interventions.[22–30] For example, studies assessing at-home compliance should probably use methodologies other than self-report, as demonstrated by a recent study incorporating nocturnal video assessment.[23] Fourth, adherence to safe sleep guidelines requires resources (eg, access to cribs that meet safety standards and secure home environments in which to use them). Consistent with past research,[31] we found that mothers of SUID cases were less educated, younger, more likely to be unmarried, and more likely to be non-Hispanic African American than those of surviving infants. These characteristics are associated with a greater likelihood of poverty, which is strongly associated with overall infant mortality,[32] preterm birth,[33] and lower compliance with safe sleep practices.[7] Thus, our findings underscore the importance of identifying population-specific challenges to the adoption of safe infant sleep practices.

Of note, we found that prenatal cigarette smoking was a strong risk factor for SUID, controlling for demographic and obstetric risk factors as well as GA. It has been well established that fetal exposure to tobacco smoke increases the risk of preterm birth[34] and SIDS.[35,36] Prenatal smoking has been associated with deficient hypoxia awakening responses[37] and attenuated recovery from hypoxemic challenges,[38] a possible explanation for their greater vulnerability and for a potentially higher burden from other risk factors, such as hazardous bedding. Multiple mechanisms can increase the risk of SIDS when the fetus is exposed to tobacco smoke. These include the occurrence of abnormalities in regions of the brainstem associated with responses to hypoxic challenges.[39–42] Education on safe infant sleep environments should address the risks of smoke exposure and ideally be implemented before conception. Although smoking throughout pregnancy increases the risk of preterm birth, quitting early reduces the risk for all but extremely preterm births.[34]

The strengths of our study include the focus on the broad category of SUID, which has become the standard measure of unexplained infant deaths in research studies and a health indicator tracked for Healthy People 2020. Another strength is the use of the linked infant birth and death certificate period files for 2012 to 2013, which captured nearly every birth and infant death in the United States, thus providing contemporary national estimates of associations between GA and SUID. These data also allowed us to incorporate important demographic, obstetric, and behavioral variables.

A limitation of our study is that the linked infant birth and death files may contain inaccuracies in the diagnosis of SUID-associated deaths because information was lacking on whether these largely unwitnessed deaths had received a death-scene investigation, which is a key component of defining SIDS.[43–45] Corrective steps were taken by the CDC with the creation of a reporting form (www.cdc.gov/sids/pdf/suidi-form2-1-2010.pdf) and the development of the SUID Case Registry (www.cdc.gov/sids/caseregistry), which enables the CDC to evaluate the use of death scene investigations in enrolled states.[45] Although 98% of cases in 7 enrolled states had conducted a death scene investigation,[45] as of 2015, only a minority of states and regions were enrolled in cooperative agreements with the Registry. Thus, the degree to which other states have comparably high rates of death scene investigation is unknown. However, because, for most cases, the diagnostic variability falls within the 3 SUID components, the use of the combined category of SUID should attenuate this limitation.[9]

A second limitation is that in 2012 to 2013, not all states reported the obstetric estimate (OE) of GA, which was phased in as states adopted the 2003 birth certificate revision. The OE, which is determined according to National Center for Health Statistics[46] birth reporting guidelines, is considered more accurate than the last menstrual period (LMP)-based measure.[47] According to a recent report, 41 states and Washington, DC reported OEs for 2013 in addition to LMP-based GAs, which all states have reported since 1981; those 41 states plus Washington, DC accounted for 90% of births in the United States in 2013, and weeks of GA were identical using the OE- and LMP-based measures for 62.1% of those births, within 1 week for 83.4%, and within 2 weeks for 91.4%.[48] Given that most states used the OE in 2012 to 2013, the high rates of agreement between the OE- and LMP-based estimates within 1 and 2 weeks, and the use of GA categories instead of individual weeks, mismeasurement of GA is unlikely a significant limitation.

Another limitation is that we were unable to directly explore the roles of sleep practices and other potential mechanisms underlying the observed association between GA and SUID. We did find that prenatal smoking, although strongly associated with SUID, did not explain any of the association between SUID and GA, and we questioned whether these findings were due to underreporting of this behavior. However, although smoking is underreported in birth records in the United States, the extent of underreporting of smoking is much lower than for most other data elements and is similar for term and preterm births.[49] Thus, the underreporting of smoking may have resulted in a conservative estimated association between smoking and SUID.

CONCLUSIONS

Despite the 2011 AAP guidelines addressing GA differences in SIDS and other sleep-related infant deaths through enhanced NICU safe infant sleep education, data from the US linked infant birth and death certificate period files for 2012 to 2013 demonstrate that an inverse relationship between GA and SUID remains. The risk for SUID associated with prematurity likely has multiple etiologies requiring continued investigation, including increased biological vulnerabilities to risk factors at earlier GAs and the efficacy of NICU education programs. Prenatal smoking, inadequate prenatal care use, and poverty-related factors were also strongly associated with SUID, suggesting that intervention strategies to reduce SUID should be multifaceted and broad-based.

ABBREVIATIONS

AAP: American Academy of Pediatrics
aOR: adjusted odds ratio
APNCU: Adequacy of Prenatal Care Utilization
ASSB: accidental suffocation and strangulation in bed
CDC: Centers for Disease Control and Prevention
CI: confidence interval
GA: gestational age
ICD-10: *International Classification of Diseases*, *Tenth Revision*
IUCM: ill-defined and unspecified causes of mortality
LMP: last menstrual period
OE: obstetric estimate
OR: odds ratio
SIDS: sudden infant death syndrome
SUID: sudden unexpected infant death

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