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Plurality of Birth and Infant Mortality Due to External Causes in the United States, 2000–2010

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Abstract

Risk of death during the first year of life due to external causes, such as unintentional injury and homicide, may be higher among twins and higher-order multiples than among singletons in the United States. We used national birth cohort linked birth–infant death data (2000–2010) to evaluate the risk of infant mortality due to external causes in multiples versus singletons in the United States. Risk of death from external causes during the study period was 3.6 per 10,000 live births in singletons and 5.1 per 10,000 live births in multiples. Using log-binomial regression, the corresponding unadjusted risk ratio was 1.40 (95% confidence interval (CI): 1.30, 1.50). After adjustment for maternal age, marital status, race/ethnicity, and education, the risk ratio was 1.68 (95% CI: 1.56, 1.81). Infant deaths due to external causes were most likely to occur between 2 and 7 months of age. Applying inverse probability weighting and assuming a hypothetical intervention where no infants were low birth weight, the adjusted controlled direct effect of plurality on infant mortality due to external causes was 1.64 (95% CI: 1.39, 1.97). Twins and higher-order multiples were at greater risk of infant mortality due to external causes, particularly between 2 and 7 months of age, and this risk appeared to be mediated largely by factors other than low-birth-weight status.

Keywords

infanticide; infant mortality; injury; multiple birth; twins

In the United States, twins and higher-order multiples are 5 times more likely than singletons to die within their first year of life (1). While the majority of infant mortality is due to pathological causes determined from factors known at birth (e.g., congenital anomalies, prematurity, low birth weight, and other complications of pregnancy), approximately 5% of infant mortality in the United States is due to external factors, such as unintentional injury and assault. It is unknown whether twins and higher-order multiples are

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at greater risk of infant mortality from external causes. However, caring for multiple infants might lead to decreased parental attention per child (2); having multiples can increase parental anxiety, stress, and depression (3, 4), particularly during the first year of life (3, 5, 6); and multiples have been found to be at higher risk of child maltreatment than singletons (7–10).

Investigation into the increased risk of death from specific preventable causes among multiples is increasingly of public health interest, as rates of twin and higher-order multiple birth have risen more than 75% over the past 3 decades (11, 12), largely attributed to the increased use of reproductive technologies and to older maternal age (13). Twins and higher-order multiples now account for 3.5% of all US births (12). In a previous study, Luke and Brown (14) described the maternal characteristics associated with potential maltreatment infant deaths among singletons and twins, separately, for US births occurring during 1995–2000. While this analysis suggested a higher risk of death due to external causes among twins compared with singletons, it included only full-term, nonanomalous, and non–low-birth-weight singletons or sets of twins, the latter of which comprised only 10% of all multiple births. Because this study was limited to infants with healthy birth characteristics, little is known about the risk due to external causes when comparing singletons with multiples overall and the contribution of adverse birth characteristics to this risk.

Our objective in the current analysis was to evaluate the risk of infant mortality due to external causes in multiples compared with singletons in the United States using the most recent decade of linked birth–infant death data available. Low birth weight has been associated with increased risk of injury-related infant death (15, 16), and multiples are more often low birth weight than singletons (12); therefore, a secondary objective of our analysis was to estimate the extent to which the effect of plurality on external causes of death is mediated outside of low-birth-weight status.

METHODS

Data were from the US 2000–2010 birth cohort linked birth–infant death vital statistics files released by the National Center for Health Statistics (NCHS) (17). These files include all US births occurring in a given year, linked with death certificate data if the infant died before his/her first birthday and both birth and death occurred within the 50 states or the District of Columbia. On average, 99% of infant death certificates were linked to their corresponding birth certificates each year. Record weights are included in the linked files to account for unlinked infant deaths; these weights upweight the infant deaths slightly but do not re-weight the births that do not result in infant death (17).

Birth certificate variables

Data on maternal and infant characteristics were obtained from the birth certificate. During 2000–2010, states were transitioning from the 1989 birth certificate to the 2003 revised birth certificate. Most of the items included in our analysis were collected in a similar or identical fashion on both versions of the birth certificate; the items which were not are described below.

Maternal characteristics, information on which the NCHS recommends be collected from the mother directly, included maternal age, race/ethnicity, marital status, education, and smoking during pregnancy (18). Maternal educational attainment at the time of delivery was recorded on the 1989 birth certificate as the highest grade completed (0– 17 years of education); in 2003, it was recorded as the highest degree or level completed (8th grade to doctorate). For our analysis, we collapsed highest grade completed from the 1989 birth certificate to 3 educational attainment categories (<12 years, 12–15 years, or 16 years), to approximately correspond with collapsed categories from the 2003 birth certificate data (less than high school, high school, bachelor’s degree or higher). Information on smoking during pregnancy was also collected differently on the 2 versions of the birth certificate. In 1989, there was an item on “tobacco use during pregnancy” (yes/no); in 2003, the number of cigarettes smoked per day was assessed by trimester, and a recoded variable for any cigarette use during pregnancy (yes/no) was calculated by the NCHS Division of Vital Statistics. Either any tobacco use or any cigarettes smoked during pregnancy was used to define smoking during pregnancy.

Infant characteristics, information on which the NCHS recommends be collected from the medical record, included plurality of birth, infant sex, birth weight, and gestational age at birth. Multiples included twins, triplets, and higher-order multiples. If a live birth was from a pregnancy that resulted in the delivery of 1 or more other fetuses, alive or dead, the live birth was identified as a multiple birth even if there were not multiple liveborn children (18); however, a live birth from a multifetal gestation resulting in the delivery of a single fetus (e.g., a “vanishing twin”) was not identified as a multiple birth. Infants who were part of a multiple set were not linked; no identifier is available from the NCHS Division of Vital Statistics for linking twins or multiple sets. Low birth weight was defined as <2,500 g (5 pounds and 8 ounces). Information on gestational age at birth was 1) calculated using the date on which the last normal menses began; 2) the clinical (“obstetric”) estimate, when the date on which last normal menses began was missing or was inconsistent with birth weight; or 3) imputed based on procedures described elsewhere (17, 19). Preterm birth was defined as a gestational age of <37 completed weeks.

Death certificate variables

Infant deaths due to external causes usually undergo a medicolegal death investigation (20). During 2003–2010, of the 94% of infant deaths due to external causes for which autopsy status was known, approximately 93% included an autopsy as part of the investigation (autopsy status was not captured for the 2000–2002 mortality data). Underlying and contributing causes of death were recorded on the death certificate by a medical examiner, coroner, or physician (21), and these open text fields were coded by mortality medical coders according to the International Classification of Diseases, Tenth Revision (ICD-10), using procedures outlined in instruction manuals provide by the NCHS (22) with the assistance of automating software (23). Age at the time of death was calculated as the difference, in days, between the dates of birth and death.

Infant mortality due to external causes was defined as ICD-10 underlying-cause-of-death codes *U01 and V01–Y84. External causes of death included accidents (unintentional

injuries; ICD-10 codes V01–X59), assault (homicide; ICD-10 codes *U01 and X85–Y09), complications of medical and surgical care (ICD-10 codes Y40–Y84), and other external causes (ICD-10 codes Y10–Y36). Because the classification of sudden unexpected infant death (SUID) includes an external cause code (accidental suffocation and strangulation in bed; ICD-10 code W75) (24, 25) and SUID has been categorized alongside external causes of death in previous analyses of “preventable-cause” or “potential mal-treatment” mortality (14, 26), we considered 3 alternative classifications of infant mortality due to external causes: external causes excluding accidental suffocation and strangulation in bed (ICD-10 codes *U01, V01–W74, and W76–Y84); external causes plus SUID (which, in addition to code W75, includes 2 pathological causes of death: sudden infant death syndrome (code R95) and other ill-defined and unspecified causes of mortality (code R99) (27)) (ICD-10 codes *U01, V01–Y84, R95, and R99); and SUID alone (ICD-10 codes W75, R95, and R99).

Statistical analysis

Pearson χ^2 tests were used to test for independence in categorical data within plurality and between singletons and multiples for selected characteristics. We fitted log-binomial models to estimate the (total effect) risk ratio for infant death due to external causes in multiples compared with singletons, pooling data across 2000–2010 to stabilize estimates. We used a causal diagram (Figure 1) to select confounders from available birth certificate variables for inclusion as covariates in these models (14, 16, 28, 29) (see Web Tables 1 and 2, available at <http://aje.oxfordjournals.org/>, for associations in our data). We did not include birth weight or gestational age as a confounder because we hypothesized that these factors might lie along the causal pathway(s) between multifetal gestation and infant death from external causes. The denominator for all analyses was total number of live births, which included infants who did not die during their first year of life and infant deaths due to pathological causes, as all liveborn infants were at risk for death due to external causes. In the regression models, applying the record weights resulted in estimates nearly identical to those from the unweighted analysis. Thus, we present unweighted results to preserve the correct number of births per year; however, for tabular display of infant death counts and percentages, we used the record weights to be consistent with other national publications on infant mortality.

We constructed curves showing the cumulative and smoothed instantaneous hazard functions for death due to external causes in multiples versus singletons over the first year of life using the Kaplan-Meier survival function estimator. Infants who died from pathological causes were censored at their age at death (in days), and surviving infants were censored at day 366. Although deaths due to pathological causes were a competing risk for deaths due to external causes, either outcome was so rare (<3%) that handling these deaths as censored observations provided reasonable approximations of the risk (30). Based on the curves generated, we performed an adhoc analysis restricting the data set to the ages at which we observed the greatest relative difference between multiples and singletons.

Mediation analysis

In order to investigate the mediating role of birth weight in the relationship between plurality and infant mortality due to external causes, we applied marginal structural models with

stabilized inverse probability weights (31, 32). We chose marginal structural modeling over other types of mediation analytical methods because we identified gestational age as both an effect of our exposure (plurality) and a confounder of the low birth weight–infant death relationship (see Figure 1). We estimated the controlled direct effect of plurality on infant death due to external causes, assuming a hypothetical scenario in which all birth weights were 2,500 g. We used logistic regression for both the exposure and the mediator weight models. The denominator model for the exposure probability weights included maternal age, race, educational attainment, marital status, sex of the infant, and smoking during pregnancy; the numerator model included no explanatory variables. The denominator model for the mediator probability weights included the maternal and infant factors mentioned above, the exposure (plurality), and an exposure-affected confounder of the relationship between the mediator and infant mortality due to external causes (gestational age of the infant at birth); the numerator model included only the exposure variable (plurality). Inverse probability weights were calculated as the product of the inverse-probability-of-exposure weight and the inverse-probability-of-mediator weight for each observation; weights were then truncated at the first and 99th percentiles (33). The final weighted marginal structural model used log-binomial regression and included an interaction term for the interaction between plurality and low birth weight, because we observed a significant negative interaction between plurality and low birth weight on both the additive and multiplicative scales (see Web Figure 1). Interpretation of the controlled direct effect as a hypothetical intervention resulting in all infants' weighing 2,500 g at birth assumed no unmeasured confounding and correct model specification. Confidence intervals were estimated using bootstrapping with 1,000 resamples.

Subgroup analysis

In order to evaluate the effect of combining information on maternal education and smoking during pregnancy from the 2 versions of the birth certificate in use during the study period, we stratified the analysis for external causes of death according to version of the birth certificate. We also stratified the analysis by maternal characteristics and year of birth to examine associations in these subgroups. The risk ratios from subgroups were then compared with the results from the main analysis, and subgroups with risk ratios higher than those seen overall were identified.

RESULTS

During 2000–2010, there were approximately 45.4 million infants born to residents of the United States; 96.7% ($n = 43,888,248$) were singletons and 3.3% ($n = 1,518,767$) were twins, triplets, or higher-order multiples (Table 1). Mothers of multiples were more likely to be older, non-Hispanic white, and married, more likely to have a bachelor's degree or higher, and less likely to have smoked during pregnancy compared with mothers of singletons (Table 1; see Web Tables 1 and 2 for maternal education and smoking data based on combined information from birth certificate revisions). Multiples were more likely than singletons to be born preterm (60% of multiples vs. 11% of singletons) and low birth weight (58% vs. 6%).

Overall, 303,936 infants (approximately 27,630 per year) died during their first year of life, which translates to 67 deaths per 10,000 live births (Table 2). On average, 3.6 per 10,000 singleton infants died from external causes during their first year of life; for multiples, the corresponding average risk was 5.1 per 10,000. However, the percentage of infant deaths from external causes was lower among multiples (1.7%) than among singletons (6.1%) due to the number of overall deaths among multiples being greater and a larger proportion of multiple deaths being attributed to pathological causes. For both singletons and multiples, characteristics associated with higher risk of infant death due to external causes were young maternal age, non-Hispanic black maternal race, unmarried maternal marital status, lower maternal educational attainment, smoking during pregnancy, earlier gestational week at birth, low birth weight, and male infant sex (Web Tables 1 and 2).

The majority of infant mortality due to external causes occurred during the postneonatal period (28–365 days of age) for both singletons and multiples (89% and 92%, respectively; $\chi^2 P = 0.03$) (Table 3). Overall, the most common manners of death were unintentional injuries (72%) and homicide (21%); the distribution of manner of death did not differ between singletons and multiples ($\chi^2 P = 0.10$). The greatest risk of death due to external causes and the greatest relative difference in risk between multiples and singletons occurred at approximately 2–7 months of life (Figure 2).

The unadjusted risk ratio for death due to external causes in multiples compared with singletons was 1.40 (95% confidence interval (CI): 1.30, 1.50) (Table 4). Adjustment for maternal factors increased this association (adjusted risk ratio (RR) = 1.68, 95% CI: 1.56, 1.81), as did restricting the analysis to ages 2–7 months (adjusted RR = 2.11, 95% CI: 1.92, 2.32). Overall, a similar association was estimated for external causes of death excluding accidental suffocation and strangulation in bed. Risk ratios were higher when SUID was combined with external cause of death or solely defined the cause of death, and were similarly increased after adjustment.

Assuming correct specification of our model and no un-measured confounding, the estimated adjusted controlled direct effect of plurality on infant death due to external causes under a hypothetical intervention in which all infants weighed 2,500 g at birth was 1.64 (95% CI: 1.39, 1.97). This estimate was similar to our overall total effect estimate, indicating that the effect of plurality on death due to external causes may be largely mediated by factors outside of low-birth-weight status. We found a somewhat different result when we combined SUID with external causes of death or when SUID solely defined the cause of death. For those outcomes, the controlled direct effect was 15%–20% lower than the estimated total effect, indicating that some of the association of plurality with infant death due to external causes and/or SUID was mediated through low birth weight.

Subgroup analyses revealed higher adjusted risk ratios for infant mortality due to external causes than overall for maternal age <25 years, non-Hispanic black maternal race, unmarried maternal marital status, maternal educational attainment of less than a bachelor's degree, the 2003 version of the birth certificate, and birth years 2003–2007 (Web Table 3).

DISCUSSION

Multiples had a 40% higher risk of death due to unintentional injuries, assault, and other external causes within the first year of life than did singletons in the United States during 2000–2010. After accounting for sociodemographic differences, the risk was 68% higher in multiples than in singletons. The greatest differences in risk occurred at approximately 2–7 months of age, where multiples were more than twice as likely to die from external causes as were singletons. Inclusion of sudden infant death syndrome and unknown cause of death, components of SUID that are not classified as external causes of death, resulted in slightly higher risk ratio estimates, which similarly increased upon adjustment. Most (>95%) of the increased risk among multiples appeared to be mediated through mechanisms operating outside of low birth weight. Because plurality of birth is not a routinely collected demographic variable and multiples are a relatively small population, infant mortality data provide one of the few nationally representative data sets available for examining the association between plurality and risk of intentional and unintentional injuries in the United States.

Our results are in agreement with those of a previous analysis of linked infant births and deaths in the United States during 1995–2000, showing that twins had a higher risk of infant mortality due to potential maltreatment than did singletons (14); however, investigators in that study excluded 90% of twins and did not examine all unintentional injury deaths or focus on the comparison of multiples with singletons. Further, analysis of the mediating effect of low birth weight was not possible because low-birth-weight infants were excluded. To the extent that our findings reflect infant death due to intentional injury, our results are consistent with previous studies which found that twins (or twin families) were at 2–20 times' higher risk of abuse than singletons in the United States and in Japan (7–10).

Our finding that the increased risk of infant mortality due to external causes in multiples appears to be primarily mediated by factors other than birth weight is novel. Direct effects of plurality on infant mortality due to external causes could include increased stress levels and divided parental attention as parents care for more than one infant at a time. As family size increases, parental attention per child diminishes (2)—twins could represent an extreme form of family growth. In addition, parents of twins experience more anxiety, stress, and depression in the children's first year of life than do parents of singletons (3, 4).

Our study was not without limitations. Potential misclassification of pathological causes of death as external causes of death could have occurred. If this type of misclassification was more common among multiples than among singletons, this could account for our observed findings. However, validation studies comparing vital records with databases of child deaths due to maltreatment have found that misclassification tends to operate in the other direction (i.e., external causes of death are more often misclassified as pathological causes (34–37)), and there is no evidence that misclassification differs by plurality. Combining information on maternal education and smoking during pregnancy from 2 different versions of the birth certificate could have led to residual confounding; however, only a modest difference in the association between plurality and infant death due to external causes was observed after stratification by birth certificate version (1989 version: adjusted RR = 1.67; 2003 version:

adjusted RR = 1.70). While additional residual confounding due to unmeasured factors could have accounted for our observed associations, adjustment for maternal factors increased our risk ratio estimates, suggesting that inclusion of additional sociodemo-graphic factors may not have attenuated our findings. In addition, we were unable to examine heterogeneity of effect estimates by type of plurality, as the number of deaths due to external causes in triplets or higher-order multiples was too small for stable estimates (there were 22 deaths among 74,920 triplets and higher-order multiples during 2000–2010). Finally, we used low birth weight as a mediator because it had previously been identified as a risk factor for injury-related infant mortality; another mediator, such as small size for gestational age, might have led to different findings.

There were several strengths of our analysis. First, linked birth–infant death data may represent the only way to assess the increased risk of death due to external causes in multiples on a national level in the United States because plurality is not included in national mortality data. In terms of national data on nonfatal injuries, plurality is not a demographic variable on which information is routinely collected (38, 39). Second, we external causes even under an assumed scenario in which there were no low-birth-weight births. This is a novel contribution to our understanding of the causes of and possible prevention measures for infant deaths due to, primarily, homicide and unintentional injury.

Our data suggest that multiples are at higher risk of potentially preventable death compared with singletons during their first year of life. Importantly, because only 2%–3% of injuries requiring medical care among infants and children are estimated to result in fatality (40, 41), it remains unknown whether multiples are at increased risk of nonfatal injuries across infancy and childhood at the national level. With the large increase in the multiple birth rate over the past 3 decades (11, 12), further examination of the higher risk of both nonfatal injuries and death due to external causes in multiples across childhood could help inform injury prevention efforts (42, 43).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

CI	confidence interval
ICD-10	International Classification of Diseases, Tenth Revision
NCHS	National Center for Health Statistics

RR	risk ratio
SUID	sudden unexpected infant death

REFERENCES

1. Matthews TJ, MacDorman MF. Infant mortality statistics from the 2010 period linked birth/infant death data set. *Natl Vital Stat Rep.* 2013;62(8):1–26.
2. Lawson DW, Mace R. Trade-offs in modern parenting: a longitudinal study of sibling competition for parental care. *Evol Hum Behav.* 2009;30(3):170–183.
3. Wenze SJ, Battle CL, Tezanos KM. Raising multiples: mental health of mothers and fathers in early parenthood. *Arch Womens Ment Health.* 2015;18(2):163–176. [PubMed: 25515039]
4. Lutz KF, Burnson C, Hane A, et al. Parenting stress, social support, and mother-child interactions in families of multiple and singleton preterm toddlers. *Fam Relat.* 2012;61(4): 642–656. [PubMed: 23125472]
5. Chang C Raising twin babies and problems in the family. *Acta Genet Med Gemellol (Roma).* 1990;39(4):501–505. [PubMed: 2102595]
6. Bryan E The impact of multiple preterm births on the family. *BJOG.* 2003;110(suppl 20):24–28. [PubMed: 12763107]
7. Ooki S Fatal child maltreatment associated with multiple births in Japan: nationwide data between July 2003 and March 2011. *Environ Health Prev Med.* 2013;18(5):416–421. [PubMed: 23558473]
8. Robarge JP, Reynolds ZB, Groothuis JR. Increased child abuse in families with twins. *Res Nurs Health.* 1982;5(4): 199–203. [PubMed: 6925853]
9. Groothuis JR, Altemeier WA, Robarge JP, et al. Increased child abuse in families with twins. *Pediatrics.* 1982;70(5): 769–773. [PubMed: 6890201]
10. Lindberg DM, Shapiro RA, Laskey AL, et al. Prevalence of abusive injuries in siblings and household contacts of physically abused children. *Pediatrics.* 2012;130(2):193–201. [PubMed: 22778300]
11. Martin JA, Hamilton BE, Osterman MJ. Three decades of twin births in the United States, 1980–2009. *NCHS Data Brief.* 2012;(80):1–8.
12. Martin JA, Hamilton BE, Osterman MJ, et al. Births: final data for 2013. *Natl Vital Stat Rep.* 2015;64(1):1–65.
13. Kulkarni AD, Jamieson DJ, Jones HW Jr, et al. Fertility treatments and multiple births in the United States. *N Engl J Med.* 2013;369(23):2218–2225. [PubMed: 24304051]
14. Luke B, Brown MB. Maternal risk factors for potential maltreatment deaths among healthy singleton and twin infants. *Twin Res Hum Genet.* 2007;10(5):778–785. [PubMed: 17903121]
15. Jain A, Khoshnood B, Lee KS, et al. Injury related infant death: the impact of race and birth weight. *Inj Prev.* 2001;7(2): 135–140. [PubMed: 11428561]
16. Brenner RA, Overpeck MD, Trumble AC, et al. Deaths attributable to injuries in infants, United States, 1983–1991. *Pediatrics.* 1999;103(5):968–974. [PubMed: 10224174]
17. National Center for Health Statistics. Vital statistics data available online. http://www.cdc.gov/nchs/data_access/Vitalstatsonline.htm. Updated October 9, 2015. Accessed June 13, 2016.
18. National Center for Health Statistics. User Guide to the 2010 Natality Public Use File. Hyattsville, MD: National Center for Health Statistics; 2012 ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/DVS/natality/UserGuide2010.pdf. Updated October 9, 2015. Accessed June 13, 2016.
19. Taffel S, Johnson D, Heuser R. A method of imputing length of gestation on birth certificates. *Vital Health Stat 2* 1982(93): 1–11.
20. Centers for Disease Control and Prevention. Public Health Law Program. Coroner/medical examiner laws, by state. <http://www.cdc.gov/phlp/publications/topic/coroner.html>. Published January 15, 2015. Accessed June 13, 2016.
21. National Center for Health Statistics. Medical Examiners' and Coroners' Handbook on Death Registration and Fetal Death Reporting. 2003 Revision. (DHHS publication no. 2003–1110).

- Hyattsville, MD: National Center for Health Statistics; 2003 http://www.cdc.gov/nchs/data/misc/hb_me.pdf. Updated April 27, 2016. Accessed June 13, 2016.
22. National Center for Health Statistics. National Vital Statistics System. Instruction manuals. http://www.cdc.gov/nchs/nvss/instruction_manuals.htm. Updated March 10, 2016. Accessed June 13, 2016.
 23. National Center for Health Statistics. National Vital Statistics System. About the Mortality Medical Data System. http://www.cdc.gov/nchs/nvss/mmds/about_mmds.htm. Published January 4, 2010. Accessed June 13, 2016.
 24. Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. Sudden Unexpected Infant Death (SUID). Atlanta, GA: Centers for Disease Control and Prevention; 2015 <http://www.cdc.gov/sids/pdf/sudden-unexpected-infant-death.pdf>. Updated June 8, 2016. Accessed June 16, 2016.
 25. National Center for Health Statistics. Infant Mortality Statistics From the 2013 Period Linked Birth/Infant Death Data Set. (National Vital Statistics Reports, vol. 64, no. 9). Hyattsville, MD: National Center for Health Statistics; 2015 http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_09.pdf. Updated June 2, 2016. Accessed June 13, 2016.
 26. Olds DL, Kitzman H, Knudtson MD, et al. Effect of home visiting by nurses on maternal and child mortality: results of a 2-decade follow-up of a randomized clinical trial. *JAMA Pediatr.* 2014;168(9):800–806. [PubMed: 25003802]
 27. Nashelsky M, Pinckard J. The death of SIDS. *Acad Forensic Pathol.* 2011;1(1):92–98.
 28. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC Med Res Methodol.* 2008;8:70. [PubMed: 18973665]
 29. Overpeck MD, Brenner RA, Trumble AC, et al. Risk factors for infant homicide in the United States. *N Engl J Med.* 1998; 339(17):1211–1216. [PubMed: 9780342]
 30. Cole SR, Hudgens MG, Brookhart MA, et al. Risk. *Am J Epidemiol* 2015;181(4):246–250. [PubMed: 25660080]
 31. Mendola P, Mumford SL, Männistö TI, et al. Controlled direct effects of preeclampsia on neonatal health after accounting for mediation by preterm birth. *Epidemiology.* 2015;26(1):17–26. [PubMed: 25437315]
 32. VanderWeele TJ. Marginal structural models for the estimation of direct and indirect effects. *Epidemiology.* 2009;20(1):18–26. [PubMed: 19234398]
 33. Cole SR, Hernán MA. Constructing inverse probability weights for marginal structural models. *Am J Epidemiol.* 2008; 168(6):656–664. [PubMed: 18682488]
 34. Crume TL, DiGuseppi C, Byers T, et al. Underascertainment of child maltreatment fatalities by death certificates, 1990–1998. *Pediatrics.* 2002;110(2):e18. [PubMed: 12165617]
 35. Ewigman B, Kivlahan C, Land G. The Missouri child fatality study: underreporting of maltreatment fatalities among children younger than five years of age, 1983 through 1986. *Pediatrics.* 1993;91(2):330–337. [PubMed: 8424006]
 36. McClain PW, Sacks JJ, Froehlke RG, et al. Estimates of fatal child abuse and neglect, United States, 1979 through 1988. *Pediatrics.* 1993;91(2):338–343. [PubMed: 8424007]
 37. Herman-Giddens ME, Brown G, Verbiest S, et al. Underascertainment of child abuse mortality in the United States. *JAMA.* 1999;282(5):463–467. [PubMed: 10442662]
 38. National Center for Health Statistics. Sample. National Ambulatory Medical Care Survey 2015 Patient Record. Hyattsville, MD: National Center for Health Statistics; 2014 http://www.cdc.gov/nchs/data/ahcd/2015_NAMCS_PRF_Sample%20Card.pdf. Updated April 18, 2016. Accessed June 13, 2016.
 39. National Center for Health Statistics. Sample. National Hospital Ambulatory Medical Care Survey 2015 Emergency Department Patient Record. Hyattsville, MD: National Center for Health Statistics; 2014 http://www.cdc.gov/nchs/data/ahcd/2015_NHAMCS_ED_PRF_Sample_Card.pdf. Updated April 18, 2016. Accessed June 13, 2016.
 40. Agran PF, Anderson C, Winn D, et al. Rates of pediatric injuries by 3-month intervals for children 0 to 3 years of age. *Pediatrics.* 2003;111(6):e683–e692. [PubMed: 12777586]
 41. Powell EC, Tanz RR. Adjusting our view of injury risk: the burden of nonfatal injuries in infancy. *Pediatrics.* 2002; 110(4):792–796. [PubMed: 12359797]

42. Stone DH, Pearson J. Unintentional injury prevention: what can paediatricians do? *Arch Dis Child Educ Pract Ed.* 2009; 94(4):102–107. [PubMed: 19654400]
43. Berger RP, Sanders D, Rubin D. Pediatricians' role in preventing child maltreatment fatalities: a call to action. *Pediatrics.* 2015;136(5):825–827. [PubMed: 26438700]

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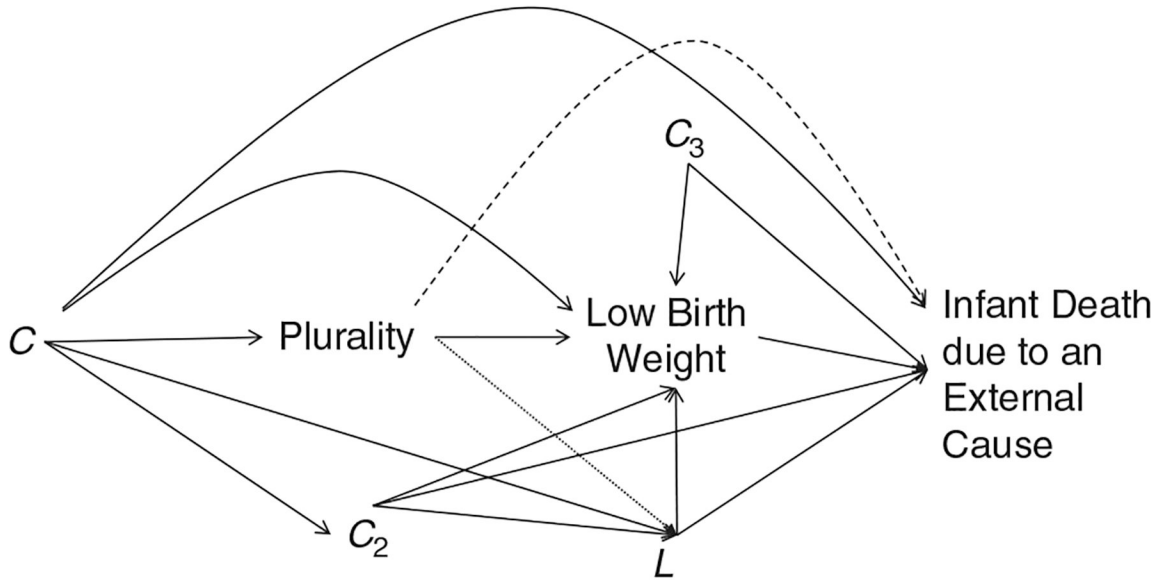


Figure 1. Hypothesized relationships between plurality of birth, low birth weight, and infant death due to external causes. A direct effect of plurality on infant death due to external causes is represented by the dashed-line arc between plurality and infant death. The dotted-line arc between plurality and a time-dependent con founder (L) highlights L as a confounding variable (C) that is also affected by exposure. C = maternal age, race, marital status, and educational attainment; C_2 = smoking during pregnancy; C_3 = sex of infant; L = gestational age of infant at birth.

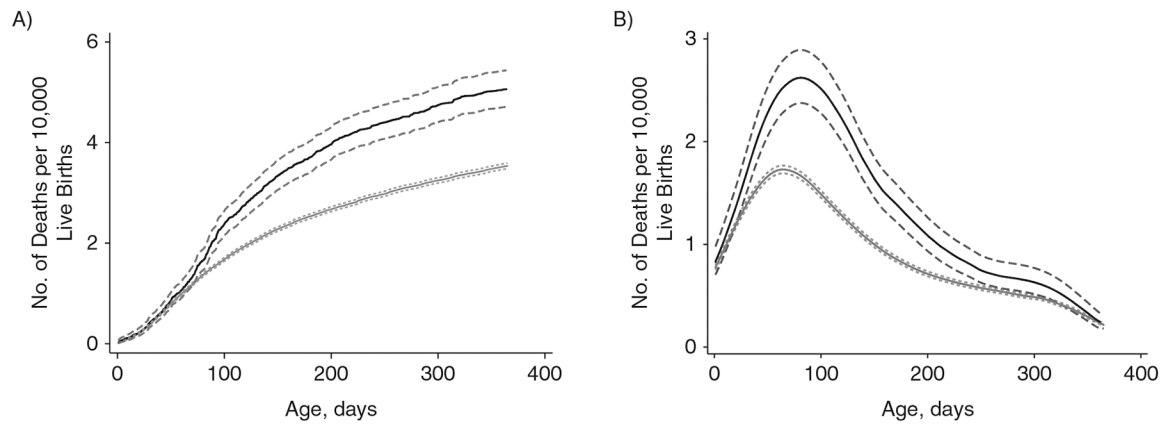


Figure 2. Cumulative (A) and smoothed instantaneous (B) hazard functions and 95% confidence intervals for infant mortality due to external causes within the first year life among multiples and singletons, United States, 2000–2010. The solid black line represents multiples (95% confidence intervals are shown with long-dashed lines); the solid gray line represents singletons (95% confidence intervals are shown with short-dashed lines).

Table 1. Selected Characteristics of Mothers and Infants According to Plurality of Birth, United States, 2000–2010

Maternal or Infant Characteristic	Total No. of Births		Singletons		Twins, Triplets, and Higher-Order Multiples ^d	
	No. of Births	%	No. of Births	%	No. of Births	%
<i>Total</i>						
Entire study period (2000–2010)	45,407,015	96.7 ^b	43,888,248	96.7 ^b	1,518,767	3.3 ^b
Entire study period (2000–2010)	4,127,911	100.0	3,989,841	100.0	138,070	100.0
<i>Average per Year</i>						
Maternal age at birth, years						
<20	429,958	10.6	423,061	10.6	6,896	5.0
20–24	1,026,351	25.1	1,002,621	25.1	23,730	17.2
25–29	1,123,429	27.3	1,088,263	27.3	35,167	25.5
30–34	952,597	22.9	912,438	22.9	40,159	29.1
35–39	476,198	11.3	451,811	11.3	24,387	17.7
40–54	119,378	2.8	111,647	2.8	7,731	5.6
Maternal race/ethnicity						
Hispanic	952,402	23.3	931,036	23.3	21,367	15.5
Non-Hispanic white	2,286,190	55.1	2,199,958	55.1	86,233	62.5
Non-Hispanic black	598,013	14.4	575,993	14.4	22,020	15.9
Other ^c	291,305	7.1	282,854	7.1	8,451	6.1
Maternal marital status at time of birth						
Not married	1,535,133	37.5	1,495,668	37.5	39,466	28.6
Married	2,592,777	62.5	2,494,173	62.5	98,604	71.4
Maternal years of education at time of birth (1989 birth certificate)						
<12	557,770	20.7	545,653	20.7	12,117	20.4
12–15	1,407,948	51.7	1,364,054	51.7	43,894	51.6
16	729,250	26.3	694,929	26.3	34,321	26.7
Not stated or unknown	35,614	1.3	34,387	1.3	1,228	1.3
Maternal educational attainment at time of birth (2003 birth certificate)						
No high school diploma or GED	304,379	22.0	297,716	22.0	6,663	21.8
High school diploma or GED	731,764	52.5	709,249	52.5	22,515	52.4

Maternal or Infant Characteristic	Total No. of Births		Singletons		Twins, Triplets, and Higher-Order Multiples ^a	
	No. of Births	%	No. of Births	%	No. of Births	%
Bachelor's degree or higher	343,794	24.2	327,259	24.2	16,535	24.6
Not stated or unknown	17,391	1.2	16,594	1.2	797	1.2
Maternal tobacco use during pregnancy (1989 birth certificate)						
No	2,163,486	79.1	2,087,928	79.1	75,557	79.2
Yes	234,963	8.7	228,829	8.7	6,134	8.6
Not stated or unknown	332,133	12.2	322,265	12.2	9,868	12.2
Maternal smoking during pregnancy (2003 birth certificate)						
No	1,004,241	71.8	969,923	71.8	34,318	71.9
Yes	119,496	8.6	116,233	8.6	3,263	8.6
Not stated or unknown	273,591	19.6	264,662	19.6	8,929	19.6
Duration of gestation at birth, weeks						
<28	30,649	0.6	23,878	0.6	6,771	4.9
28–31	50,831	1.0	39,682	1.0	11,150	8.1
32–35	235,832	4.8	192,155	4.8	43,677	31.6
36	187,087	4.1	165,499	4.1	21,588	15.6
37–39	2,168,836	53.2	2,121,921	53.2	46,915	34.0
40	805,491	20.1	801,984	20.1	3,507	2.5
41	372,258	9.3	370,631	9.3	1,627	1.2
42	250,574	6.2	248,595	6.2	1,979	1.4
Unknown or not stated	26,352	0.6	25,496	0.6	856	0.6
Birth weight, g						
<1,500	61,333	1.1	45,310	1.1	16,023	11.6
1,500–2,499	270,904	5.2	206,445	5.2	64,459	46.7
2,500	3,794,651	93.7	3,737,129	93.7	57,522	41.7
Unknown or not stated	1,023	0.0	957	0.0	66	0.0
Sex						
Female	2,015,466	48.8	1,946,884	48.8	68,582	49.7
Male	2,112,445	51.2	2,042,957	51.2	69,487	50.3

Abbreviation: GED, General Educational Development.

^aIncluded 95.1% twins, 4.6% triplets, and 0.3% other multiples.

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^bRow percent.

^cIncluded Asian or Pacific Islander, American Indian or Alaska Native, other, and persons for whom Hispanic origin was unknown or not stated.

Table 2.

Distribution of Infant (Age <1 Year) Deaths According to *International Classification of Diseases, Tenth Revision*, Grouping and Plurality of Birth, United States, 2000–2010

ICD-10 Grouping	ICD-10 Codes	All Infant Deaths			Deaths of Singletons			Deaths of Twins, Triplets, and Higher-Order Multiples		
		No. of Deaths ^a	No. per 10,000 Births	% of Deaths	No. of Deaths ^a	No. per 10,000 Births	% of Deaths	No. of Deaths ^a	No. per 10,000 Births	% of Deaths
Total		303,936	66.9	100.0	258,406	58.9	100.0	45,531	299.8	100.0
External causes	U01 and V01-Y84	16,631	3.7	5.5	15,865	3.6	6.1	766	5.1	1.7
External causes, excluding accidental suffocation and strangulation in bed	U01, V01-W74, and W76-Y84	10,692	2.4	3.5	10,201	2.3	3.9	491	3.2	1.1
External causes and SUID	U01, V01-Y84, R95, and R99	53,504	11.8	17.6	50,509	11.5	19.5	2,996	19.7	6.6
SUID only	R95, R99, and W75	42,812	9.4	14.1	40,307	9.2	15.6	2,505	16.5	5.5

Abbreviations: ICD-10, *International Classification of Diseases, Tenth Revision*; SUID, sudden unexpected infant death.

^aWeighted infant death count (see text).

Table 3.

Distribution of Infant (Age <1 Year) Deaths Due to External Causes, According to Selected Infant Death Characteristics and Plurality of Birth, United States, 2000–2010

Infant Death Characteristic	Total No. of Deaths Due to External Causes ^d	External-Cause Deaths Among Singletons		External-Cause Deaths Among Twins, Triplets, and Higher-Order Multiples	
		No. of Deaths ^d	%	No. of Deaths ^d	%
Total	16,632	15,865	100.0	766	100.0
Age at death, days					
<7 (early neonatal death)	579	555	3.5	24	3.1
7–27 (late neonatal death)	1,196	1,159	7.3	37	4.8
28–365 (postneonatal death)	14,857	14,151	89.2	705	92.0
28–90 (early postneonatal death)	5,558	5,302	33.4	256	33.4
91–182 (early-middle postneonatal death)	4,737	4,486	28.3	250	32.6
183–273 (late-middle postneonatal death)	2,635	2,517	15.9	118	15.4
274–365 (late postneonatal death)	1,927	1,846	11.6	81	10.6
External cause of mortality					
Accidents (unintentional injuries)	11,941	11,403	71.9	538	70.2
Transport accident	1,378	1,344	11.8	34	6.3
Falls	187	179	1.6	8	— ^b
Firearms	5	5	—	0	—
Drowning/submersion	595	574	5.0	20	3.7
Accidental suffocation and strangulation in bed	5,939	5,663	49.7	276	51.4
Other strangulation/suffocation	2,049	1,947	17.1	102	19.0
Obstruction of respiratory tract	662	619	5.4	44	8.2
Smoke, fire, flames	332	318	2.8	14	2.6
Poisoning	179	170	1.5	9	—
Other ^c	615	585	5.1	30	5.6
Assault (homicide)	3,457	3,290	20.7	167	21.8
Complications of medical and surgical care ^d	217	200	1.3	17	2.2
Other external causes ^e	1,016	971	6.1	44	5.7

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Abbreviation: ICD-10, *International Classification of Disease, Tenth Revision*.

^aWeighted infant death count (see text). Numbers may not sum to totals because of rounding.

^bPercentage did not meet National Center for Health Statistics standards of reliability or precision.

^cThe most frequent ICD-10 codes for other accidents across the study period (2000–2010) included: exposure to unspecified factor (code X59; *n* = 206); exposure to excessive heat (code X30; *n* = 130); caught, crushed, or jammed in or between objects (code W23; *n* = 89); and struck by thrown, projected, or falling object (code W20; *n* = 45).

^dThe most frequent ICD-10 codes for complications of medical or surgical care across the study period (2000–2010) included: surgical operation and other surgical procedures as the cause of abnormal reaction of the patient, or of later complication, without misadventure at the time of the procedure (code Y83; *n* = 87); and other medical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure (code Y84; *n* = 77).

^eThe most frequent ICD-10 codes for other external causes across the study period (2000–2010) included: hanging, strangulation, and suffocation of undetermined intent (code Y20; *n* = 496); unspecified event of undetermined intent (code Y34; *n* = 243); other specified event of undetermined intent (code Y33; *n* = 77); and drowning and submersion of undetermined intent (code Y21; *n* = 53).

Table 4. Risk of Infant Death According to *International Classification of Diseases, Tenth Revision*, Grouping and Plurality of Birth, United States, 2000–2010

ICD-10 Grouping and Plurality of Birth	ICD-10 Codes	No. of Live Births	No. of Deaths ^a	Total Effects			Controlled Direct Effect (Adjusted 2 ^c)		
				Unadjusted	Adjusted 1 ^b	RR	95% CI	RR	95% CI
External causes	U01 and Y01-Y84								
Singletons		43,888,248	15,726	1	Referent	1	Referent	1	Referent
Twins, triplets, and higher-order multiples		1,518,767	760	1.40	1.30,1.50	1.68	1.56,1.81	1.64	1.39, 1.97
External causes, excluding accidental suffocation and strangulation in bed	U01, Y01-W74, and W76-Y84								
Singletons		43,888,248	10,110	1	Referent	1	Referent	1	Referent
Twins, triplets, and higher-order multiples		1,518,767	486	1.39	1.27,1.52	1.68	1.53,1.84	1.63	1.34, 1.95
External causes and SUID	U01, Y01-Y84, R95, and R99								
Singletons		43,888,248	50,057	1	Referent	1	Referent	1	Referent
Twins, triplets, and higher-order multiples		1,518,767	2,969	1.71	1.65,1.78	2.04	1.97,2.12	1.70	1.57, 1.84
SUID only	R95, R99, and W75								
Singletons		43,888,248	39,947	1	Referent	1	Referent	1	Referent
Twins, triplets, and higher-order multiples		1,518,767	2,483	1.80	1.72, 1.87	2.13	2.05, 2.22	1.71	1.58, 1.87

Abbreviations: CI, confidence interval; GED, General Educational Development; ICD-10, *International Classification of Diseases, Tenth Revision*; RR, risk ratio; SUID, sudden unexpected infant death.

^aUnweighted infant death count.

^bIn adjusted model 1, covariates included maternal age (<20, 20–24, 25–29, 30–34, 35–39, or 40–54 years), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, other), education (no high school diploma or GED, high school diploma or GED, bachelor’s degree or higher, not stated or unknown) and marital status (married, unmarried).

^cAdjusted model 2 used inverse probability weighting for low birth weight as a mediating variable, controlling for the covariates in adjusted model 1 and sex of the infant, smoking during pregnancy, and infant’s gestational age at birth. The controlled direct effect of plurality not mediated through birth weight was estimated using marginal structural models for a hypothetical intervention in which all birth weights were 2,500 g. RRs were estimated using weighted log-binomial regression, with bootstrapping used to estimate 95% CIs.