BACKGROUND: Reductions in sudden infant death syndrome (SIDS) are commonly attributed to modifications in infant sleep environments. Approaches to diagnosis in sudden infant death, death scene investigations, the prevalence of intrinsic risk factors for SIDS, and the potential influence of treatment-related factors on infant vulnerability have also changed. Understanding all contributory factors may help reduce residual SIDS rates.

METHODS: We analyzed US Mortality Multiple Causes Records for 1983 to 2012 to compare SIDS postneonatal mortality rates with a projection applying non-SIDS mortality changes, using those changes as a proxy measure for alterations in intrinsic risk. Composites of neglect-related, unknown, and circumstantial respiratory diagnoses were measured, as was a cumulative composite of unexplained infant death diagnoses. Cluster analysis with leading causes of postneonatal mortality and SIDS mortality rates for low birth weight infants were also examined.

RESULTS: SIDS and non-SIDS postneonatal mortality rates were concordant over time. Important variance was seen 1994 to 1996, coinciding with Back-to-Sleep initiation. Other variance, eliminated in the cumulative composite, appeared related to differences in diagnostic practices. Changes in SIDS rates resembled changes in mortality from congenital malformations, respiratory distress of the newborn, and diseases of the circulatory system. SIDS rates for low birth weight infants followed broader postneonatal trends.

CONCLUSIONS: SIDS mortality followed trends in overall postneonatal mortality, including effects of changes in the infant sleep environment and diagnostic classification. Preventing asphyxia risk in the sleep environment must be coupled with efforts to understand intrinsic biological pathways, some potentially associated with other categories of infant and perinatal mortality.

WHAT'S KNOWN ABOUT THIS SUBJECT: A major etiologic model proposes that SIDS occurs in infants with latent biological vulnerabilities when exposed to external threats during a critical developmental period. Reductions in SIDS mortality are broadly attributed to changes in the infant sleep environment.

WHAT THIS STUDY ADDS: SIDS mortality reductions showed concordance with known causes of postneonatal mortality. These findings suggest that efforts addressing the sleep environment must be coupled with understanding intrinsic biological pathways, some potentially associated with other categories of infant and perinatal mortality.

Approximately 4000 infants die suddenly without an immediately apparent cause each year in the United States. The final diagnosis in more than half of these deaths is sudden infant death syndrome (SIDS), “the sudden and unexpected death of an infant under 12 months of age that remains unexplained after a review of the clinical history, complete autopsy, and death scene investigation.” Typically, SIDS deaths are unwitnessed and occur during sleep or in transitions between sleep and arousal. Biomarkers are not available to aid in the diagnosis of SIDS, a diagnosis made by exclusion during a forensic investigation. SIDS is the leading cause of postneonatal mortality and the fourth leading cause of infant mortality in the United States. Back-to-Sleep (BTS) initiatives directed at infant sleep position and environment, promoted by the American Academy of Pediatrics and the National Institute of Child Health and Development, led to decreases in the prevalence of prone infant sleep from 70% to 24% in the United States from 1992 to 1996, while reported SIDS rates decreased by 38%. Mortality reductions from SIDS have stalled for more than a decade, with only modest recent improvements despite ongoing public health efforts to affect the sleep environment and strategies aimed at high-risk groups.

Investigations of unexplained death have also changed since that time, with standardized death scene investigations promising better ascertainment of lethal infant sleep environments. Research has also demonstrated diagnostic shift, the use of alternative diagnostic coding reflecting a putative or uncertain role for asphyxia or sleep environment risk, without formal consensus on alternatives to the term SIDS. Medical examiners have been advised to use different terms than SIDS when sleep environment risk factors for SIDS are found. Not all infant deaths considered due to SIDS before the promotion of BTS are diagnosed as SIDS now. Recent nomenclature proposals attempt to conceptually reframe the diagnosis to quantify the certainty of asphyxiation. Although associations between SIDS rates and changes in the sleep environment or nomenclature have been systematically examined, the relationship between SIDS and broader trends in infant mortality has not. A major etiologic hypothesis for SIDS, the Triple Risk Model, explains SIDS as occurring through interactions between underlying intrinsic vulnerability, a critical developmental period, and extrinsic factors in the infant’s environment, including prone sleep position, overbundling, bedding surfaces, and bed-sharing. A major premise in basic science-based SIDS research today is that the intrinsic vulnerability of some infants reflects underlying neural or systemic abnormalities in homeostatic control, impairing responses to life-threatening challenges during sleep, such as hypoxia, hypercarbia, and thermal or autonomic stress. The Triple Risk model posits that SIDS infants have underlying pathophysiology. We reason that the pathophysiology of SIDS may be affected by some of the same factors also contributing to mortality from known causes of infant death.

Intrinsic risk presents as biological vulnerability caused by factors with a genetic, developmental, or environmental basis affecting susceptibility to SIDS, including African American race, male gender, preterm birth, and prenatal tobacco or alcohol use, in contrast to an extrinsic physical stressor around the time of death in the vulnerable infant. Changes have occurred in these intrinsic risks over time. Direct alterations to risk are illustrated in decreased maternal tobacco use, decreased teenage births, improved prenatal care, and increased breastfeeding. Indirect alterations may also have occurred through evolving medical interventions associated with improved survival in the postneonatal period. For example, approximately one-third of infants dying of SIDS have a history of prematurity, and BTS was promoted during the same years when antenatal steroids and surfactant achieved broad implementation.

In general, reductions in SIDS rates may result from changes in extrinsic factors related to the sleep environment, changes in the classification of postneonatal deaths likely to affect the SIDS diagnostic category, changes in the constellation of known intrinsic risks for SIDS, or changes in factors affecting intrinsic or extrinsic risks likely to influence SIDS in the postneonatal period. Indeed, a combination of factors is probably involved. In this study, we developed a measure to consistently account for infants whose death would have been considered due to SIDS over the entire study period: the Cumulative Unexplained Infant Death (CUID) Composite. Hypothesizing that concordance between CUID and non-SIDS postneonatal mortality rates reflects trends in intrinsic factors affecting SIDS rates unrelated to the sleep environment, we tested projected mortality rates for SIDS had they followed patterns of mortality changes in known causes of postneonatal death. The analysis asked what would have happened to SIDS mortality rates if they had changed in accordance with all other causes of postneonatal mortality, causes of death unaffected by recommended changes in the infant sleep environment, in the time before, during, and after the initiation of the BTS campaign. Finally, we looked for comparable mortality trends in other leading causes of infant death, as well as SIDS mortality trends in infants at elevated risk for SIDS, seeking additional evidence of

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common influences shared by SIDS and non-SIDS causes of mortality.

METHODS

Data

We used US Mortality Multiple Causes Records from the National Center for Health Statistics for 1983 to 2012. The 30-year period was chosen because it began before the initiation of the BTS initiatives and continued until the most recently available data. For subanalysis investigating low birth weight (LBW) and SIDS, we used Linked Birth–Infant Death Records. Linked data records are available after 1994 and were not produced for 1992 to 1994 because of programmatic transitions. Years before 1992 were obtained by combining birth cohort linked files for 1984 to 1991. A complete data set could not be obtained for 1983.

Definitions

We used the International Classification of Diseases, Ninth Revision (ICD-9) for deaths before 1999 and Tenth Revision (ICD-10) for deaths since 1999 (Table 1). SIDS diagnosis increased as cause of death in ICD-10 because it was ignored when better-defined conditions were documented in ICD-9 (comparability ratio 1.0362), although not sufficiently to affect analysis. To examine trends in diagnostic reallocation relevant to SIDS, we developed 3 composites of related codes: External Causes Composite, Unknown Composite, and Circumstantial Respiratory Composite. We developed the External Causes Composite to include specific neglect-related diagnoses that potentially increased because of better ascertainment from standardized death scene investigations and should not properly be included among SIDS deaths. The Unknown Composite was developed to capture diagnoses without attributable cause in deaths similar to SIDS, when there may have been reluctance to use the term SIDS. The Circumstantial Respiratory Composite included deaths where specific evidence was lacking, but the conclusion was asphyxia in an otherwise normal infant, also SIDS substitute codes. The CUID Composite included SIDS, Unknown Composite, Circumstantial Respiratory Composite, and other causes lacking specific evidence, to monitor the consistent category of unexplained postneonatal deaths without established, specific causes.

Statistical Analysis

Cause-specific mortality rates per 1000 live births per year were calculated for SIDS and non-SIDS infant (0–12 months) and postneonatal (1–12 month) deaths. Subsequent analysis focused on postneonatal deaths because historically >90% of SIDS occurs in the postneonatal period. Non-SIDS mortality rate was calculated as total mortality rate minus SIDS mortality rate. Absolute and relative changes in all rates were calculated for the average of the 1983 to 1985 and 2010 to 2012 periods. We compared trends in SIDS with the diagnostic composites.

We calculated a projected annual rate for SIDS based on annual changes in non-SIDS mortality, multiplying the SIDS rate of year a by the percentage change in non-SIDS mortality rates from year a to year b, to determine the projected SIDS rate for year b (where a is the year preceding b). This method was repeated for the CUID Composite. Concordance between actual and projected rates for CUID was assessed with a Bland–Altman plot. It plotted the difference between the actual and projected CUID rates against the average of the actual and projected rates, depicting the average difference and the 95% limits of agreement for this difference. The average and 95% confidence intervals excluded years of hypothesized excess mortality reduction (1994–1996). We confirmed a normal distribution of these differences.

To consider the relationship of SIDS trends to explained causes of infant death, we conducted a hierarchical cluster analysis with an agglomerative (bottom-up) approach, squared Euclidean distance, and average linkage, comparing SIDS trends with other leading causes of infant mortality: Congenital malformations, deformations and chromosomal abnormalities; Disorders related to short gestation and LBW, not elsewhere classified; Newborn affected by maternal complications of pregnancy; Accidents; Newborn affected by complications of placenta, cord and membranes; Bacterial sepsis of newborn; Respiratory distress of newborn; Diseases of the circulatory system; and Neonatal hemorrhage.

Finally, we examined whether an increase in LBW infants surviving the neonatal period was accompanied by an increase in SIDS because of the survivors’ higher risk for SIDS and the declines in competing causes of mortality. To consider this relationship, we examined birth weight–specific SIDS mortality rates for LBW infants over the 30-year period and compared them with a birth weight–specific projected annual rate, determined similarly to the SIDS projection described earlier.

Data analysis was performed with SAS version 9.3 (SAS Institute, Inc, Cary, NC), and plots drawn in Microsoft Excel 97–2003 (Microsoft Corporation, Redmond, WA).

RESULTS

A total of 947 156 infant deaths occurred between 1983 and 2012. Table 1 presents trends in SIDS and non-SIDS postneonatal mortality.
between 1983 to 1985 and 2010 to 2012. The SIDS rate in 2010 to 2012 was 32.3% of the rate in 1983 to 1985. Over the 30-year period, the SIDS postneonatal infant mortality rate decreased 71.3% from 1.357 per 1000 live births (4902 deaths) to 0.390 per 1000 live births (1534 deaths), whereas SIDS infant mortality decreased 70.9% from 1.458 (5305 deaths) to 0.425 per 1000 (1679 deaths). Non-SIDS postneonatal mortality decreased from 2.552 per 1000 to 1.586 per 1000, a 37.9% reduction, and non-SIDS infant mortality decreased from 9.707 per 1000 to 5.553 per 1000, a 42.8% decline (Fig 1A).

The External Causes Composite increased by 9.3% from 0.007 to 0.008 per 1000. Mortality in the Circumstantial Respiratory Composite increased by 0.148 per 1000 (272.2%), 96% of the increase after 1992. The Unknown Composite increased by 0.110 per 1000 (92.3%), 81% after 1997. The CUID Composite declined 44% in parallel to SIDS from 1988 to 1998, and was relatively flat after 1998, a period corresponding to 29% of the decline in SIDS rates during the study period (Fig 1B).

The curves comparing projected with actual SIDS rates largely overlapped (Fig 2A). Actual SIDS reductions exceeded the projection in 1994 to 1996, 1998 to 2001, and 2012. Reductions in mortality rates were not found after 1998, when the CUID Composite was used instead of SIDS (Fig 2B). The Bland–Altman plot using the CUID Composite (Fig 3) found the predictive model within the 95% confidence interval in 26 of 30 years (≤0.08 cases per 1000 live births). The years outside the 95% confidence interval included 1994 to 1996, as hypothesized, and 1986, when actual SIDS mortality was higher than predicted.

Cluster analysis (Fig 4) showed that changes in SIDS rates were most similar to changes in congenital malformations, deformations,
and chromosomal abnormalities; respiratory distress of the newborn; and diseases of the circulatory system. Mortality rates increased or remained largely unchanged in other categories. Analysis of birth weight–specific SIDS mortality showed concordance through the 30-year period, with a reduction in mortality in all birth weight groups.

Unavailability of matched data 1992 to 1994 prohibited testing during that period (Fig 5).

**DISCUSSION**

In this study of postneonatal mortality over 3 decades, SIDS rates declined 71.3%. Declines associated with BTS were evident after its initiation (1994–1996), when the SIDS postneonatal mortality rate declined 33.5%. As hypothesized, however, we also found substantial concordance between SIDS rates and that of all other causes of postneonatal mortality. This concordance averaged to within 0.01 cases per 1000 births over the 30-year period. Diagnostic shift was illustrated by the CUID Composite rates, which did not decline after 1998 but followed broader postneonatal mortality trends, despite reported decreases in SIDS rates until 2001 and again after 2009. These later reductions in SIDS rates were largely offset by increases in diagnoses included in the Circumstantial Respiratory and Unknown Composites, codes reflecting a lack of known, specific cause that arguably were once considered and called SIDS. The External Composite did not demonstrate the identification of significantly more neglect-related deaths with greater adoption of standardized death scene investigations.
It has been recognized that SIDS mortality has decreased since inclusion in the International Classification of Diseases in 1973, decades before the promotion of supine sleep positioning. Without diminishing the remarkable contributions of BTS, this 30-year analysis raises important considerations that changes in mortality were also associated with concurrent influences on postneonatal mortality and those affecting intrinsic risk. Although it has been noted that all-cause postneonatal mortality has followed a trend similar to SIDS, the interrelationship has received little attention. The use of specific-cause mortality as a proxy for intrinsic SIDS risk is an untested strategy, and the relationship between concurrence and causation is speculative. Nonetheless, SIDS mortality trends are highly concordant with predictions in the model used in this study. Additional support that SIDS and non-SIDS mortality share common influences is provided by the cluster analysis, where SIDS mortality trends most closely follow specific conditions with improvements attributable to advances in prenatal and neonatal care. Additionally, SIDS mortality did not increase in LBW infants over the study period, despite the greater numbers of survivors of LBW with

Decreases in known intrinsic risk factors for SIDS over this period are a credible contribution to the concordance. Rates of smoking during pregnancy decreased from 16.0% in 1987 to 10.2% in 2011, for example, and initiated breastfeeding increased from 56.3% to 83.9%. In addition, developments such as the use of antenatal steroids, which tripled from 1991–1999, leading to reductions in respiratory distress of the newborn and intraventricular hemorrhage, may also have played a role in reducing SIDS mortality rates. Similarly, increasing access to prenatal care over the study period, with its potential to affect adverse intrauterine environments, reducing risk for intrauterine growth retardation and preterm birth in particular (themselves risks for SIDS), is another plausible influence on intrinsic risk. Although other changes in extrinsic risk, not just BTS, may be contributory rather than beneficial effects on shared natural disease-related precursors or their treatments, the concordance with the prediction is striking. Moreover, the discovery of biological causes in what was once considered SIDS, including abnormalities in cardiac, metabolic, or neural systems, should also inform our understanding of the role of intrinsic factors in SIDS mortality.

Diagnostic shift illustrates the complex interplay between medical science, forensic practice, and epidemiology. Although some changes in diagnostic preferences may reflect attitudes toward particular nomenclature, such as the use of “cause unknown” instead of “SIDS,” others imply significant differences in the decision-making process for the classification of sudden infant deaths. The increased use of “accidental suffocation and strangulation in bed” instead of “SIDS,” for example, reflects awareness of potentially lethal asphyxial conditions from improved scene investigations but also debatable judgments about their contribution to death in an assumed normal infant. Increases in the Circumstantial Respiratory Composite after 1992 may reflect an increasingly prevalent assumption about the role of asphyxia when determining cause of death in the BTS era. Increases in the Unknown Composite, clear after 1997, may relate to discourse around death scene investigation and ensuing stringency or reluctance to use “SIDS” as a diagnosis. These nomenclature issues will continue to require vigilance in assessing historical patterns of SIDS.

A limitation of this study is the potential to incorrectly infer that population-based correlations operate at the level of individual and specific diagnosis (ecological fallacy). However, our argument here is not to supplant the conventional view of SIDS rate reductions as related importantly to changes in infant sleep practices but to suggest that this view is incomplete. Although the pathogenesis of SIDS is largely understood in terms of factors of external risk, there have also been relevant changes in intrinsic risk and vulnerability. Moreover, the concordance of our predictive model
provides caution that an exclusive focus on extrinsic risk reduction may miss possible interventions in intrinsic risk reduction as an approach to decreasing the incidence of SIDS. An additional potential limitation of the study is that our comparisons between SIDS and non-SIDS postneonatal mortality rates do not identify specific shared risks. Available national data provide few relevant variables (eg, breastfeeding, prenatal care, maternal smoking) and thus do not permit detailed assessment of potential shared medical or other risks. Still, this study underscores the potential for such shared influences and outlines the scale of their possible impact, areas for future research. Also, missing years of linked data correspond to the years of clearest BTS effects, making analysis of declines in those years impossible in this, but also all other, SIDS mortality studies using national statistics. Finally, misclassification error due to variations in cause of death determination is a limitation also shared with all other US studies of SIDS rates. Death certification does not require autopsy or standardized death scene investigation, and there is marked heterogeneity in investigations and the performance of autopsies in infant deaths by medical examiner systems across the country. Inadequate resources and facilities, and a lack of specialized expertise, and technical infrastructure also contribute. However, determining whether death is due to known causes or SIDS is part of the daily determination by medical examiners in unexpected infant deaths.

CONCLUSIONS

Pediatricians should be clear about the importance of safe infant sleep environments, just as they continue to stress the importance of reducing maternal smoking and increasing breastfeeding to prevent SIDS. Our study and others suggest that estimated reductions generally attributed to BTS may have been overstated because of changes in diagnostic terminology. We found that accounting for changes in the relevant terminology by using categories of unexplained or equivocally explained death not currently called SIDS, and including these deaths with SIDS, diminishes measured declines. Importantly, the resulting measure of SIDS deaths significantly follows decreases in death from known causes, suggesting common influences such as reductions in perinatal risk factors and improved perinatal care. Future progress in understanding these factors will depend on wider consensus on nomenclature, attention to contributory prenatal and neonatal factors, continued review of environmental factors, and biological research on SIDS and its complex etiologies.

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ABBREVIATIONS

BTS: Back-to-Sleep
CUID: Cumulative Unexplained Infant Death
ICD-9: International Classification of Diseases, Ninth Revision
ICD-10: International Classification of Diseases, Tenth Revision
LBW: low birth weight
SIDS: sudden infant death syndrome

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