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Causes of neonatal and postneonatal death among infants with birth defects in Texas

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Abstract

Background: The proportion of deaths attributed to various causes has not been quantified among infants with birth defects. We sought to describe the causes of neonatal and postneonatal death among infants in the Texas Birth Defects Registry.

Methods: We calculated frequencies and percentages for both underlying causes and all causes (underlying or contributing) of neonatal (0–27 days) and postneonatal (28–364 days) death listed on death certificates among infants born alive with birth defects and delivered in Texas during 1999–2013 (n = 8,389 deaths). Analyses were repeated separately for infants with isolated, multiple, and syndromic defects.

Results: After birth defects, the most frequently listed causes of neonatal death were preterm/low birth weight (10%), circulatory system diseases (8%), and sepsis (5%). The leading postneonatal

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CONFLICT OF INTEREST

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causes of death beyond birth defects were circulatory system diseases (32%), sepsis (11%), and renal failure (7%).

Conclusions: Improved understanding of the causes of mortality among infants with birth defects may help identify priorities for postnatal care. Our results suggest that potentially modifiable causes of death (e.g., circulatory system diseases, sepsis) contribute substantially to mortality in this population. Prioritizing continued improvements in prevention, diagnosis, and management of preventable conditions may reduce mortality among infants born with birth defects.

Keywords

birth defects; cause of death; epidemiology; infant mortality; registries

1 | INTRODUCTION

Birth defects affect about 3% of infants in the United States (US), and an estimated 5–8% of live born infants with birth defects will die in infancy, compared to approximately 0.6% of live born infants in the US (Agha, Williams, Marrett, To, & Dodds, 2006; Centers for Disease Control and Prevention [CDC], 2008; Heron, 2019; Texas Department of State Health Services, 2013). Infants with a birth defect have an increased likelihood of being born preterm or low birthweight (Baer et al., 2019; Miquel-Verges, Mosley, Block, & Hobbs, 2015; Rasmussen, Moore, Paulozzi, & Rhodenhiser, 2001; Swanson & Sinkin, 2013) and developing necrotizing enterocolitis (NEC) and sepsis (Ascher et al., 2012; Fullerton et al., 2017; McElhinney et al., 2000; Spinner et al., 2020). For some defects, surgery and extended hospital-based care may be necessary, increasing the risk of surgery-related complications and nosocomial infections (CDC, 2007; Adams-Chapman et al., 2013; Colvin & Bower, 2009; Moffitt, Case, Farag, & Canfield, 2016). All of these factors contribute to the increased risk of mortality among infants with birth defects.

While the majority of death certificates among infants with birth defects list the birth defect itself as the underlying cause of death (e.g., congenital heart defect; Copeland & Kirby, 2007), there are other potentially modifiable contributing causes of death (e.g., sepsis) that increase the risk of mortality in this population. Preventing these conditions among infants with birth defects and improving management when they do occur may reduce mortality; however, the proportion of deaths to which various causes contributed has not been quantified among infants with birth defects. Better understanding the common causes of death among infants with birth defects may improve understanding of the broader population impact, as well as help to identify opportunities for improving postnatal care, facilitating resource planning, and identifying research priorities. Consequently, our objectives were to describe the leading underlying and contributing causes of neonatal and postneonatal death among infants born with birth defects and evaluate differences in the causes of death among infants with isolated, multiple, or syndromic defects. To do so, we conducted a retrospective cohort study to tabulate both underlying and contributing causes of death among infants with birth defects in Texas.

2 | METHODS

Data for this study were obtained from the Texas Birth Defects Registry (TBDR) and the Center for Health Statistics at the Texas Department of State Health Services. The TBDR conducts active surveillance in hospitals, birthing centers, and hospital-based clinics around the state to ascertain birth defects among live births, fetal deaths, and terminations (Miller, 2006). Mothers must reside in Texas at the time of delivery to be included in the TBDR. Ascertained birth defects are coded using modified British Pediatric Association (BPA) codes based on standardized protocols and diagnoses are either "definite" or "possible or probable." The protocol for this study was approved by the Institutional Review Board of The University of Texas Health Science Center at Houston.

Analyses were restricted to live born, singleton infants in the TBDR delivered between 1999 and 2013 with at least one definite, major birth defect recorded. Infants with a documented syndromic diagnosis, including chromosomal abnormalities, were identified through BPA codes and review of the text description of the ascertained defects. BPA codes considered to be minor defects based on criteria established by the National Birth Defects Prevention Study (Rasmussen et al., 2003) and clinicians at the TBDR were excluded from analyses. The remaining BPA codes among infants without an identified syndrome were then grouped by the first four digits and infants were coded as having either an isolated defect (one unique major 4-digit BPA code present) or multiple defects (more than one unique major 4-digit BPA code present; Benjamin et al., 2019).

Records in the TBDR are routinely linked to vital records (birth certificates, death certificates, and fetal death certificates) from the Vital Statistics Section at the Texas Department of State Health Services. For infants with a linked death certificate, we calculated the number of days alive by subtracting the date of birth from the date of death. Among infants that died within the first year, we classified deaths as occurring during the neonatal (0–27 days) or postneonatal (28–364 days) period, given differences in causes of mortality between these periods. Maternal and infant characteristics were collected via vital records or abstracted from medical records by the TBDR and data on causes of death were obtained from linked death certificates. Death certificates listed the causes of death according to the Tenth Revision of the International Statistical Classification of Diseases (ICD-10; CDC, 2020). There is one field for the underlying cause of death, described as the disease or injury that initiated the chain of events leading to death, as well as additional fields listing contributing causes of death (CDC, 2004).

2.1 | Analyses

Maternal and infant characteristics were tabulated and proportions were calculated by outcome: neonatal death, postneonatal death, or survival to 1 year. Kaplan–Meier survival curves were generated for the full sample and by defect classification group (isolated, multiple, or syndromic). We conducted a log-rank test to assess differences in the survival curves over the first year by defect classification group.

Counts and proportions for the underlying causes of death, classified according to the National Center for Health Statistics (NCHS) 71 ranked causes of infant death categories

(CDC, 2020), were calculated separately for neonatal and postneonatal deaths. The rank for each cause was determined. For comparison, we abstracted the rank for that cause among the 10 leading causes of neonatal and postneonatal death reported for deaths among all live births in the US population in 2017 (Heron, 2019). Counts and proportions were also calculated for all causes of death, either underlying or contributing, listed on death certificates. All analyses were conducted among infants with all birth defects, then repeated separately for infants classified into isolated, multiple, and syndromic defect categories.

Due to the large number of deaths within the "congenital malformations" cause of death category, we also evaluated more detailed subgroups within that category by tabulating the NCHS 130 causes of infant death, which categorizes birth defects into more detailed subgroups (e.g., "congenital malformations of heart"), and individual ICD-10 codes (e.g., "gastroschisis" within the "congenital malformations and deformations of musculoskeletal system, limbs and integument" category; CDC, 2020). We additionally conducted post hoc analyses tabulating counts and proportions for all causes of death among infants with circulatory system disease and sepsis (either "bacterial sepsis of newborn" or "septicemia") listed as an underlying or contributing cause of death in order to quantify the co-occurring causes of death among these specific infants. Finally, we conducted a post hoc analysis to calculate the proportion of infants that were preterm (gestational age < 37 weeks) among (a) infants with lung hypoplasia (ICD-10 Q33.6) listed among the underlying or contributing causes of death and (b) infants with NEC (ICD-10 P77) listed among the underlying or contributing causes of death. All analyses were conducted in SAS version 9.4 (SAS Institute Inc., Cary, NC).

3 | RESULTS

There were 173,871 eligible live born, singleton infants delivered between 1999 and 2013 with one or more major defects or a syndromic diagnosis recorded in the TBDR. Among these infants, 8,389 (4.8%) died within the first year of life; 5,097 (61%) deaths occurred during the neonatal period (0–27 days) and 3,292 (39%) deaths occurred during the postneonatal period (28–364 days).

Infants with birth defects born to black or Hispanic mothers were less likely to survive infancy as compared to infants born to mothers of white or other race/ethnicity (Table 1). Infants born to younger or older mothers (<20 or ≥40 years of age) were less likely to survive infancy as compared to infants born to mothers between 20 and 39 years of age (Table 1). Additionally, a larger proportion of female infants and preterm infants (gestational age < 37 weeks) died during the neonatal and postneonatal time periods (Table 1). Infants with three or fewer causes of death listed on the death certificate were more likely to have died during the neonatal period, while infants with four or more causes of death listed were more likely to have died during the postneonatal period compared to the proportion of deaths in each period for the overall cohort (Table 1).

First year survival significantly differed by defect classification group (i.e., isolated, multiple, or syndromic defects; log-rank test for equality of the survival curves $p < .001$). Infants with isolated malformations had the highest first year survival (98.4%), while 93.1%

of infants with multiple malformations survived the first year, and infants with syndromic malformations had the lowest first year survival (83.8%). Differences in first year survival curves over time are shown in the Kaplan–Meier plot (Figure 1).

3.1 | Neonatal causes of death

The leading underlying causes of neonatal death are shown in Table 2, with the corresponding rank among the top 10 causes of neonatal death among all live births in the US in 2017 (Heron, 2019). Sepsis, atelectasis, and NEC ranked higher in Texas neonates with birth defects (second, third, and seventh place) than among all live births in the US population (fifth, 10th, and ninth place, respectively; Table 2). Diseases of the circulatory system and hydrops fetalis (fifth and eighth most frequently listed underlying causes in our analysis) did not appear in the top 10 causes of neonatal death in the US in 2017 (Heron, 2019). Focusing on all listed causes of death (Table 3), preterm/low birthweight was the second most frequently listed cause of neonatal death after birth defects, present on the death certificate in 10% of neonatal deaths, followed by diseases of the circulatory system (8%), sepsis (5%), intrauterine hypoxia (5%), and atelectasis (5%).

The distributions of specific causes of neonatal death differed by defect classification group (Table 3). Among all causes of death listed on death certificates, infants with isolated malformations had the lowest proportion of neonatal deaths that included birth defects among the cited causes (62%), while infants with syndromic defects had the highest proportion (92%). Looking at subgroups within congenital malformations, heart defects were listed among the causes of neonatal death for 36% of infants with multiple malformations, but were less frequently listed among infants with isolated and syndromic malformations (7% and 20%, respectively). Diaphragmatic hernia was listed as a cause of neonatal death more often in nonsyndromic infants (8–9%) than in infants with syndromic defects (3%), while lung hypoplasia affected infants across all three defect classification groups (listed among the contributing causes of neonatal death in 11–21% of deaths in each group). Anencephaly was the single largest cause of death among isolated cases, accounting for nearly a quarter of the neonatal deaths (24%) in that group. Circulatory system diseases and intrauterine hypoxia were more frequently included among the causes of death for infants with multiple defects (12% and 7%, respectively) compared to infants with an isolated (9% and 5%) or syndromic defect (5% and 4%).

3.2 | Postneonatal causes of death

Circulatory system disease, septicemia, and chronic respiratory disease originating in the perinatal period ranked higher as underlying causes of postneonatal death among infants with birth defects than among live births in the US population (second, third, and fifth place vs. fourth, eighth, and ninth place, respectively). Seven of the top 10 underlying causes of postneonatal death were the same as those reported among all live births in the US population (Table 2), while three of the leading underlying causes of postneonatal death among infants with birth defects were not among the leading causes among all live births in the US population: gastritis, duodenitis, and noninfective enteritis and colitis (seventh), diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (ninth), and renal failure and other disorders of kidney (10th). For postneonatal

deaths, birth defects were listed among all causes of death in 67% of infants (Table 3). The other leading causes of postneonatal death listed in the largest proportion of deaths included diseases of the circulatory system (32%), septicemia (11%), preterm/low birthweight (9%), renal failure (7%), and influenza and pneumonia (5%; Table 3).

Examining specific causes of postneonatal death by defect classification group, isolated cases had the lowest proportion of deaths with birth defects listed among the causes of death (31%) and infants with syndromic defects had the largest proportion (79%). Heart defects were the most frequently listed subgroup, cited in 45% of deaths among infants with multiple malformations and 35% of deaths among infants with syndromic defects. Circulatory system diseases were frequently listed across all defect classification groups (25% of isolated, 39% of multiple, and 29% of syndromic). Septicemia (9–12% of deaths) and renal disorders/failure (5–8% of deaths) were also frequently cited across all the groups, while preterm/low birthweight was disproportionately listed as a cause of death among infants with isolated defects (18%) compared to infants with multiple (10%) and syndromic (5%) defects. Additionally, approximately 3–4% of deaths in all groups listed complications of medical or surgical care among the causes of death.

3.3 | Post hoc analyses

Among 1,443 infants that had circulatory system diseases listed among the causes of death during either the neonatal or postneonatal period, the most frequently specified types of circulatory disorders were pulmonary hypertension (n = 346, 24%), cardiac arrest (n = 255, 18%), and hypotension (n = 153, 11%). Congenital heart defects were the most common type of birth defect listed among the causes of death (n = 574, 40%) and 144 infants (10%) had “other congenital malformations of circulatory system” (ICD-10 codes Q25-Q28; e.g., atresia or stenosis of the aorta or pulmonary artery) listed. The next most frequently listed birth defect category was “congenital malformations and deformations of the musculoskeletal system, limbs and integument” (ICD-10 codes Q65-Q85), which was listed on 129 death certificates (9%). Hypoplastic left heart syndrome was the most frequently specified heart defect (n = 86, 6%) and congenital diaphragmatic hernia was the most frequently specified musculoskeletal defect (n = 75, 5%).

Among 641 infants that had either “bacterial sepsis of newborn” (ICD-10 code P36) or “septicemia” (ICD-10 code A40-A41) listed among the causes of neonatal or postneonatal death, congenital heart defects were listed on 165 (26%) death certificates and 44 (7%) had “congenital malformations and deformations of the musculoskeletal system, limbs and integument” (ICD-10 codes Q65-Q85). Hypoplastic left heart syndrome was again the most frequently specified heart defect (n = 23, 4%), while gastroschisis was the most frequently specified musculoskeletal defect (n = 16, 2%).

As compared to 55% of infants delivered preterm among all infants that died during the first year of life (Table 1), 64% of the 953 infants with lung hypoplasia and dysplasia listed among the causes of death were preterm. Among 157 infants with NEC listed among the causes of death, 76% were preterm.

4 | DISCUSSION

Consistent with prior findings, infants with birth defects experienced high mortality in our study, with about 5% of infants dying before their first birthday. In this comprehensive analysis of causes of death among a cohort of live born infants with any major birth defect, we identified several causes of death (e.g., circulatory system diseases, sepsis) that were frequently listed among the underlying or contributing causes of death in this cohort and ranked higher as an underlying cause of death in this population compared to all live births in the US population. These findings suggest that these factors contribute substantially to the sequence of events leading to death among infants with birth defects, and therefore may represent potential pathways by which mortality could be reduced.

When considering both underlying and contributing causes of death listed on death certificates, 8% of neonatal and 32% of postneonatal deaths cited circulatory system diseases. Circulatory system diseases are associated with congenital heart defects, the most common group of birth defects, as well as diaphragmatic hernia, and lung hypoplasia (Abman et al., 2015; Hansmann, 2017). Our results were consistent with prior literature, as heart defects, lung hypoplasia, and congenital diaphragmatic hernia were each frequently co-listed on death certificates with circulatory system diseases. Heart defects and circulatory system diseases were more frequently listed among the causes of death for infants with multiple defects than infants with an isolated defect. This may suggest that heart defects co-occurring with other defects may be more susceptible to subsequent circulatory system complications. Although some circulatory system causes represent the terminal event in the sequence of events leading to death (e.g., cardiac arrest), continuing to improve monitoring of hemodynamics in at-risk infants, promoting early recognition of decompensation prior to cardiac arrest, and strengthening the evidence base on various treatment modalities could result in a reduction in infant mortality given the high proportion of infant mortality related to circulatory system diseases (Marino et al., 2018; Vrancken, van Heijst, & de Boode, 2018).

Sepsis was listed among the contributing causes of death in over 5% of neonatal and 10% of postneonatal infant deaths. We found that heart defects and gastroschisis were the most frequently cited birth defects co-listed with sepsis. Again, these findings were consistent with previous literature (Ascher et al., 2012; Fullerton et al., 2017), and our results highlight sepsis prevention and improved treatment among infants with birth defects as a potential priority area to target for reducing mortality. Further work related to identifying the specific events involved in postnatal sepsis occurrence (e.g., surgical complications) may help to better understand this burden of mortality. Interventions to prevent sepsis among infants with birth defects and reduce the case fatality rate when it does occur could have a substantial impact on infant mortality in this population.

Several other frequently listed causes of death were related to lung and respiratory development and function (listed among the causes of death in 4–5% of neonatal and 4% of postneonatal infant deaths). These conditions, such as atelectasis (incomplete lung expansion), respiratory distress of the newborn, chronic respiratory disease, and lung hypoplasia (listed within the congenital malformation category), could be due to prematurity

and/or may be related to anomalies affecting diaphragm and lung development preventing adequate lung development and expansion (Dominguez & Alvares, 2018; Gallacher, Hart, & Kotecha, 2016). Similarly, both preterm birth and birth defects are associated with NEC, which ranked higher as a cause of death in our study population than among all live births in the US population (Fullerton et al., 2017; McElhinney et al., 2000; Rose & Patel, 2018; Spinner et al., 2020). In our study, a higher proportion of infants with lung hypoplasia/ dysplasia and NEC listed among the causes of death were born preterm compared to the preterm proportion in the overall cohort of infants with birth defects that died during the first year of life. Continued efforts to study ways to reduce preterm birth could also positively impact infant mortality among infants with birth defects, where the compound effects of prematurity/ low birthweight and the presence of birth defects complicate postnatal care and increase the risk of death.

Consistent with the annually reported results among all live births in the US population, we observed major differences between the causes of death during the neonatal and postneonatal periods. Neonatal deaths were more likely than postneonatal deaths to list congenital malformations, preterm and preterm-associated causes (e.g., NEC, respiratory distress), and conditions specifically affecting neonates (e.g., neonatal hemorrhage) as both underlying and contributing causes of death. Postneonatal deaths included circulatory system diseases, infections (e.g., influenza and pneumonia), renal failure/ disease, and accidents much more frequently than neonatal deaths.

We also observed differences between the causes of death by defect classification. Infants with isolated defects (one major birth defect code listed in the TBDR) were much less likely than infants with multiple or syndromic defects to have birth defects listed as a cause of death during the postneonatal period. Infants with isolated defects that survive the neonatal period tend to have better outcomes compared to infants with multiple defects or syndromes (Nembhard, Waller, Sever, & Canfield, 2001; Wang, Hu, & Druschel, 2010).

The strengths of our study included the use of a large, diverse population-based registry with active surveillance and linkages to state vital records data. We were able to assess the mortality experience of this cohort of infants with sufficient numbers to compare to the causes of death among all live born infants in the US population. While there are many methods available to classify perinatal and infant deaths, we used data available on US Standard Death Certificates and the standard categories for causes of infant death used by the NCHS, which are reported annually for the US population. This method allowed for grouping causes into distinct, broad categories. We also looked at select subgroups by tabulating counts for more specific birth defect categories, allowing us to examine these deaths in greater detail. As with other cause of death studies that utilize death certificate data, there may be inconsistencies in assigning underlying and contributing causes of death. Research has shown discrepancies between the underlying causes of death listed on death certificates and clinical summaries from medical records and these discrepancies may vary with the level of training of the certifier and the location of death (hospital vs. nonhospital setting; Myers & Farquhar, 1998; McGivern,Shulman, Carney, Shapiro, & Bundock, 2017). Despite the possibility of misclassifying some causes of death, death certificate data provide statewide data collected in a standard manner; a clinical cohort or case series would not

provide the large, diverse, population-based sample we were able to evaluate. Our analyses also relied on vital records linkages and some deaths may have been missed due to out-of-state deaths or an inability to link registry cases to the corresponding death certificate due to missing or inaccurate data for linking variables. The expected impact was likely relatively low, as previous work in the Texas Birth Defects Registry has shown that supplementing mortality analyses with linkages to the National Death Index looking at 5-year mortality resulted in few additional deaths (Marengo, Hoyt, & Canfield, 2014).

5 | CONCLUSION

We examined the underlying and contributing causes of death among infants born with birth defects with the goal of quantifying mortality attributed to various causes. Strategies to reduce the occurrence and improve the management of conditions that contribute substantially to mortality in this population could have a significant impact on birth defects mortality. Our results highlight how pervasive infant mortality related to circulatory system diseases and sepsis is among infants with birth defects, and thus suggest that improved interventions (e.g., targeting prevention, early diagnosis, and management of these conditions) may represent impactful candidates to prioritize for future research and management.

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DATA AVAILABILITY STATEMENT

The data analyzed are not publicly available due to confidentiality of vital records.

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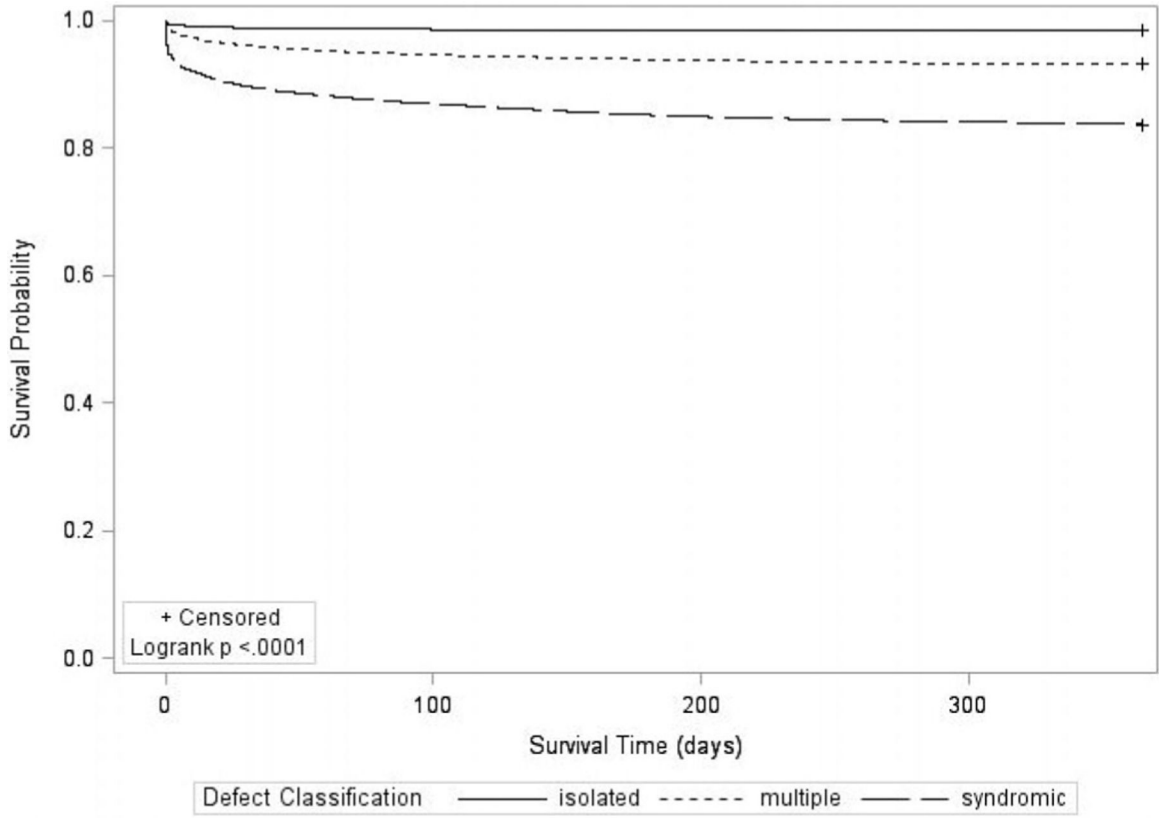

FIGURE 1.

Kaplan–Meier survival curve for the first year of life by defect classification, Texas Birth Defect Registry, 1999–2013 deliveries

TABLE 1

Characteristics of live born infants in the Texas Birth Defects Registry by first year survival status, 1999–2013 deliveries

Maternal/infant characteristic	Neonatal death (0–27 days; *n* = 5,097)	Postneonatal death (28–364 days; *n* = 3,292)	Survived infancy (≥365 days; *n* = 165,482)
Maternal race/ethnicity			
White non-Hispanic	1,651 (2.7)	1,004 (1.6)	59,562 (95.7)
Black non-Hispanic	581 (2.9)	517 (2.6)	18,636 (94.4)
Hispanic	2,674 (3.1)	1,672 (2.0)	81,158 (94.9)
Other	189 (3.0)	99 (1.6)	6,079 (95.5)
Maternal age (years)			
<20	797 (3.4)	549 (2.3)	22,094 (94.3)
20–29	2,525 (2.8)	1,656 (1.8)	86,843 (95.4)
30–39	1,520 (2.8)	927 (1.7)	51,487 (95.5)
≥40	254 (4.6)	160 (2.9)	5,050 (92.4)
Education			
Less than high school	1,657 (3.3)	1,112 (2.2)	47,696 (94.5)
High school	1,524 (3.0)	1,042 (2.0)	48,397 (95.0)
Greater than high school	1,753 (2.5)	1,106 (1.6)	67,757 (96.0)
Infant sex			
Male	2,701 (2.8)	1,728 (1.8)	93,686 (95.5)
Female	2,359 (3.1)	1,561 (2.1)	71,721 (94.8)
Gestational age (weeks)			
<28	728 (14.8)	317 (6.4)	3,879 (78.8)
28–31	681 (10.8)	281 (4.5)	5,324 (84.7)
32–36	1,717 (6.3)	841 (3.1)	24,636 (90.6)
≥37	1,959 (1.4)	1,850 (1.4)	131,381 (97.2)
Defect classification			
Isolated malformation[a]	1,189 (1.1)	611 (0.5)	109,676 (98.4)
Multiple malformations[b]	1,431 (3.8)	1,162 (3.1)	35,193 (93.1)
Syndromic malformations	2,477 (10.1)	1,519 (6.2)	20,613 (83.8)
Number of causes of death listed			
1	1,314 (65.4)	695 (34.6)	Not applicable

Maternal/infant characteristic	Neonatal death (0–27 days; *n* = 5,097)	Postneonatal death (28–364 days; *n* = 3,292)	Survived infancy (≥365 days; *n* = 165,482)
2	1,599 (66.3)	814 (33.7)	
3	1,178 (61.2)	747 (38.8)	
4	608 (53.9)	521 (46.1)	
≥5	398 (43.6)	515 (56.4)	
Birth year			
1999–2003	1,597 (3.4)	999 (2.2)	43,758 (94.4)
2004–2008	1,738 (2.9)	1,175 (2.0)	56,988 (95.1)
2009–2013	1,762 (2.6)	1,118 (1.7)	64,736 (95.7)

[a] One major birth defect recorded (grouped by four-digit British Pediatric Association code).

[b] More than one major birth defect recorded (grouped by four-digit British Pediatric Association code).

TABLE 2

Leading underlying causes of neonatal and postneonatal death among infants in the Texas Birth Defects Registry, 1999–2013 deliveries

Rank[a]	Underlying cause of death (ICD-10 code)	*n*	%	US population rank[b]
Neonatal (0–27 days)				
1	Congenital malformations, deformations, and chromosomal abnormalities (Q00–Q99)	3,797	74.5	2
2	Bacterial sepsis of newborn (P36)	107	2.1	5
3	Atelectasis (P28.0–P28.1)	95	1.9	10
4	Newborn affected by maternal complications of pregnancy (P01)	90	1.8	3
5	Diseases of the circulatory system (I00–I99)	82	1.6	NA
5	Disorders related to short gestation and low birth weight (P07)	82	1.6	1
7	Necrotizing enterocolitis of newborn (P77)	78	1.5	9
8	Hydrops fetalis not due to hemolytic disease (P83.2)	76	1.5	NA
9	Neonatal hemorrhage (P50–P52, P54)	60	1.2	7
10	Respiratory distress of newborn (P22)	52	1.0	6
...	All other causes	578	11.3	
...	All causes	5,097	100.0	
Postneonatal (28–364 days)				
1	Congenital malformations, deformations, and chromosomal abnormalities (Q00–Q99)	1,825	55.4	1
2	Diseases of the circulatory system (I00–I99)	212	6.4	4
3	Septicemia (A40-A41)	95	2.9	8
4	Sudden infant death syndrome (R95)	93	2.8	2
5	Chronic respiratory disease originating in the perinatal period (P27)	77	2.3	9
6	Accidents (unintentional injuries) (V01–X59)	60	1.8	3
7	Gastritis, duodenitis, and noninfective enteritis and colitis (K29, K50–K55)	43	1.3	NA
8	Influenza and pneumonia (J10–J18)	41	1.2	7
9	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50–D89)	37	1.1	NA
10	Renal failure and other disorders of kidney (N17–N19, N25, N27)	26	0.8	NA
...	All other causes	783	23.8	
...	All causes	3,292	100.0	

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; NA, not available.

[a]Underlying cause of death rank; top 10 causes during each time period shown.

[b] Rank of underlying neonatal or postneonatal cause of death among all live births in the US population from table 2 in Heron (2019).

TABLE 3

Leading underlying and contributing causes of neonatal and postneonatal death among infants in the Texas Birth Defects Registry (multiple causes per infant possible), overall and by defect classification, 1999–2013 deliveries

			Defect classification[c]		
Rank[a]	**Cause of death (ICD-10 code)[b]**	**Overall %[c]**	**Isolated %[d]**	**Multiple %[e]**	**Syndromic %**
Neonatal (0 to < 28 days)					
1	Congenital malformations, deformations, and chromosomal abnormalities (Q00–Q99)	81.9	61.5	82.1	91.6
	Congenital malformations of heart (Q20–Q24)	*21.8*	*7.1*	*36.3*	*20.4*
	Chromosomal abnormalities (Q90–Q99)	*18.6*	*0.0*	*0.0*	*38.3*
	Congenital malformations of respiratory system (Q30–Q34)	*18.5*	*11.9*	*17.3*	*22.4*
	Congenital hypoplasia and dysplasia of lung (Q33.6)	*17.0*	*11.1*	*15.7*	*20.6*
	Congenital malformations and deformations of musculoskeletal system, limbs and integument (Q65–Q85)	*13.8*	*12.4*	*12.9*	*15.0*
	Congenital diaphragmatic hernia (Q79.3)	*5.9*	*8.0*	*9.2*	*3.0*
	Congenital malformations of genitourinary system (Q50–Q64)	*11.8*	*4.0*	*7.8*	*17.8*
	Anencephaly and similar malformations (Q00)	*7.1*	*23.5*	*5.1*	*0.4*
2	Disorders related to short gestation and low birth weight, not elsewhere classified (P07)	9.5	11.9	8.5	8.8
3	Diseases of the circulatory system (I00–I99)	7.8	8.7	11.8	5.0
4	Bacterial sepsis of newborn (P36)	5.4	10.3	6.0	2.6
5	Intrauterine hypoxia and birth asphyxia (P20–P21)	5.1	5.1	7.1	4.0
6	Atelectasis (P28.0–P28.1)	4.6	5.1	4.9	4.1
7	Respiratory distress of newborn (P22)	4.0	5.9	3.4	3.6
8	Neonatal hemorrhage (P50–P52, P54)	3.9	8.0	5.4	1.2
9	Newborn affected by maternal complications of pregnancy (P01)	3.7	5.0	2.7	3.8
10	Hydrops fetalis not due to hemolytic disease (P83.2)	3.0	4.4	3.8	1.9
Postneonatal (28 to < 365 days)					
1	Congenital malformations, deformations, and chromosomal abnormalities (Q00–Q99)	67.1	30.6	70.7	79.0
	Congenital malformations of heart (Q20–Q24)	*33.4*	*7.2*	*44.8*	*35.1*
	Chromosomal abnormalities (Q90–Q99)	*15.5*	*0.0*	*0.0*	*33.5*
	Other congenital malformations of nervous system (Q01–Q02, Q04, Q06–Q07)	*7.5*	*6.2*	*8.9*	*7.0*
	Congenital malformations and deformations of musculoskeletal system, limbs and integument (Q65–Q85)	*7.0*	*6.2*	*6.7*	*7.6*
	Congenital diaphragmatic hernia (Q79.0)	*2.0*	*3.6*	*3.0*	*0.6*

Rank[a]	Cause of death (ICD-10 code)[b]	Overall %[c]	Defect classification[c]		
			Isolated %[d]	Multiple %[e]	Syndromic %
2	Diseases of the circulatory system (I00–I99)	31.7	24.9	38.6	29.2
3	Septicemia (A40–A41)	10.5	12.4	12.0	8.6
4	Disorders related to short gestation and low birth weight, not elsewhere classified (P07)	9.1	18.2	9.6	5.1
5	Renal failure and other disorders of kidney (N17–N19, N25, N27)	6.5	6.9	7.7	5.4
6	Influenza and pneumonia (J10-J18)	5.3	5.4	4.6	5.9
7	Chronic respiratory disease originating in the perinatal period (P27)	3.7	6.9	3.7	2.5
8	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50–D89)	3.5	2.8	3.2	4.1
9	Gastritis, duodenitis, and noninfective enteritis and colitis (K29, K50–K55)	3.4	7.4	3.7	1.5
10	Complications of medical and surgical care (Y40–Y84)	3.1	2.8	3.9	2.6

Abbreviation: ICD-10, International Classification of Diseases, 10th revision.

[a] Rank among all listed causes of death (any mention among underlying or contributing causes); top 10 most frequently listed causes during each time period shown.

[b] Italicized listings indicate subgroups from the National Center for Health Statistics (NCHS) 130 causes of infant death and italicized indented listings indicate an individual ICD-10 code within the subgroup.

[c] Percentage of deaths in which the cause was listed as an underlying or contributing cause of death; totals do not sum to 100% due to cases having multiple contributing causes of death listed.

[d] One major birth defect recorded (grouped by four-digit British Pediatric Association code).

[e] More than one major birth defect recorded (grouped by four-digit British Pediatric Association code).