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Analysis of the Burden of Infant Mortality due to Birth Defects by Race/Ethnicity in the United States from 2010-2014

By

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Master of Public Health

Epidemiology

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Abstract

Analysis of the Burden of Infant Mortality due to Birth Defects by Race/Ethnicity in the United States from 2010-2014

By Avinash Joseph

Congenital anomalies, also known as birth defects, are among the leading contributors to infant mortality each year in the United States. The proportion of infant mortality due to birth defects has been shown to vary by race and/or ethnicity, with Hispanics and Asians having the highest risk. The purpose of this analysis was to determine the current burden of infant mortality due to birth defects, and racial and ethnic disparities associated with it among all infant deaths in the United States. We examined the National Vital Statistics System Linked Birth/Death data files for the most recent 5 years, 2010 through 2014. Proportional mortality due to birth defects was then calculated for five racial/ethnic groups: Non-Hispanic White, Non-Hispanic Black, Hispanic, American Indian, and Asian, further stratified by birth weight and age at death. Differences in characteristics between deaths due to birth defects and all other causes were compared using the Chi-square test. Cochran-Armitage test was used to examine trends in birth defects associated infant mortality across the 5-year period. We observed that significant differences exist in mortality due to birth defects by race and ethnicity (Chi-square=1591.71, $p<0.0001$), with proportional mortalities of 25.86% for Hispanics, 22.99% for Non-Hispanic Whites, 22.09% for Asians, 20.40% for American Indians, and 13.32% for Non-Hispanic Blacks. The test for trend showed a significant decrease in proportional mortality for Non-Hispanic Blacks (P value=0.0300) and Hispanics (P value=0.0407) over the 5-year period. Proportional mortalities across birth weight and age at death categories also showed racial/ethnic differences with a few aberrations, such as Hispanics having a relatively low proportion of birth defects associated mortality at extremely low birth weights and Asians having a relatively high proportion when age at death was between 28 and 365 days. In summary, our analysis demonstrates that racial/ethnic disparities are persistent in infant mortality due to birth defects across birth weight and age at death categories and have not changed in the recent years compared to previous years. We recommend further research into understanding infant mortality associated with birth defects and addressing preventable mortality.

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LITERATURE REVIEW

Congenital malformations, commonly known as birth defects, are a leading cause of infant mortality in the United States, accounting for approximately 20% of infant deaths (1). Among babies that survive with birth defects there is a large burden of morbidity and under-5 mortality, accounting for 12% of pediatric hospitalizations and 2.3% of premature death and disability in the United States, measured by disability-adjusted life years (2). Birth defects encompass a wide variety of structural and functional abnormalities that can appear in newborns. Structural defects include problems such as cleft lip or palate, heart defects, abnormal limbs, and neural tube defects. Functional abnormalities include nervous system or brain problems (i.e. Down syndrome, seizure disorders, etc.), sensory problems, metabolic problems (i.e. phenylketonuria), and degenerative disorders (i.e. muscular dystrophy). Birth defects are relatively common worldwide, diagnosed in approximately 6% of live births (1). The prevalence of birth defects varies significantly by country and region. Industrialized countries have much lower rates of serious or fatal birth defects than developing countries. The causes of birth defects are complex and largely multifactorial. These causes can be broadly stratified into three groups: genetic causes (approximately 40% of birth defects), non-genetic causes (approximately 10% of birth defects), and unknown causes (approximately 50% of birth defects) (3). Genetic causes can be further subdivided into chromosomal abnormalities, single-gene defects, and multifactorial causes. Non-genetic causes can also be classified further into teratogen caused (harmful environmental exposures during pregnancy) and constraint caused (physiological pressure in utero leading to deformation of the fetus) (3). The relatively common nature of birth defects may be due to the large number of diseases

that fall under the congenital disorder umbrella. Serious birth defects account for the fifth most years of potential life lost in the United States. Birth defects also account for a large portion of healthcare spending (2). Not only is immediate care for neonates with potentially fatal birth defects expensive, but also long term care for children with less immediately serious birth defects (i.e. neural tube defects or chromosomal defects leading to behavioral issues) can accumulate significant cost over the course of the child's lifetime.

Causes of birth defects

Chromosomal abnormalities are one of the genetic causes of birth defects (4). Chromosomal abnormalities occur during the process of reproduction and can present in several different ways. One way is an abnormal number of chromosomes in the cells. Occasionally during gamete formation, a pair of chromosomes does not split properly, leading to an abnormal number of chromosomes in the gamete. If this gamete is then utilized for reproduction, the zygote will contain either one too many chromosomes (trisomy) or one too few chromosomes (monosomy). Trisomy can cause a number of different birth defects, including Down syndrome, Edward syndrome and extra sex-chromosome related disorders (i.e. XXY or XYY in a male). The most common trisomy-caused birth defect is Down syndrome, a non-fatal disorder that causes intellectual disability. The third form of abnormal chromosome number is called mosaicism. Mosaicism occurs early in the zygote's normal mitotic division and results in one cell having 47 chromosomes (trisomy) and the other having 45 chromosomes (monosomy). Normally the monosomy cell dies off but the trisomy cell survives, leading to some cells having a normal number of chromosomes and some cells having an abnormal number.

The disorders that result from mosaicism heavily overlap with those that result from trisomy (i.e. Down syndrome, Turner syndrome).

Birth defects can also be caused by abnormalities at a single gene (4). Single gene defects are caused by mutations to the structure of the gene. These mutations can occur spontaneously or through a variety of epigenetic factors such as radiation or DNA methylation. Some common autosomal single gene defects include polydactyly, dwarfism, sickle cell anemia, and thalassemia. The most common sex-linked single gene defects are red-green color blindness and hemophilia. As these defects are due to a mutation in only a single gene, it is more common for them to vary significantly across distinct populations and subgroups.

Some birth defects have a multifactorial etiology. Multifactorial birth defects result from more than one factor, a combination of genetic and environmental exposures. The etiology of these birth defects is normally sequential: an inherited gene or sequence of genes leaves the offspring susceptible to a later environmental exposure that causes the birth defect (5). Multifactorial birth defects are more common than other genetic causes of birth defects. Among the most common multifactorial birth defects are categories such as neural tube defects (spina bifida, anencephaly, etc.) and congenital heart defects.

Teratogens, or harmful environmental exposures to the fetus, differ from multifactorial birth defects in that a genetic factor does not need to be involved. The term teratogen is very loose and can apply to everything from ingested alcohol to radiation to infection. The effect of teratogens varies based on the stage of development the fetus occupies. Teratogens tend to do the most damage immediately following implantation of the zygote in the uterus, as the development of the placenta provides a conduit from the

mother for potentially deleterious substances to affect the development of the fetus (3). At this stage, organ systems are still developing and are most vulnerable to teratogens. The most common examples of teratogens are maternal infection or illness (ie. Rubella, toxoplasmosis, diabetes), excessive radiation, drug use (both recreational and prescribed), and environmental toxins.

Constraint refers to external pressure that produces a birth defect in an otherwise normally formed fetus. Deformities refer to mechanical pressure exerted in utero that normally correct themselves after the baby has been born. Occasionally, an amniotic band causes permanent damage to the fetus by damaging a limb or other part of the body. This type of birth defect is known as a disruption and is less common than deformities.

Infant Mortality

Infant mortality refers to the death of a child within the first year of life. Infant mortality rate is considered an important marker of overall health of a country or region, and a significant indicator of health inequity among different ethnicities and countries. Worldwide developing countries tend to have much higher rates of infant mortality than the industrialized world. This is due to a wide variety of factors, including healthcare delivery systems, infrastructure, diet, prenatal care, and others. Within the United States, racial and ethnic minority groups tend to have higher rates of infant mortality than Non-Hispanic Whites do (6).

There are several potential causes for infant mortality, but three causes make up the vast majority of infant mortality cases. The first (and most common) of these causes is low birth weight. Low birth weight is defined by the World Health Organization as a

baby weighing less than 2,500 grams at birth (1). There are two main reasons for low birth weight: premature birth and fetal growth restriction. Premature birth refers to any birth occurring before 37 weeks of gestation, while fetal growth restriction refers to a fetus that does not attain the weight it should before birth. There are myriad potential reasons for a low birth weight, ranging from smoking during pregnancy to infection to maternal age (7). While some of these risk factors can be controlled, others (such as race/ethnicity) cannot. Birth defects themselves are often linked to low birth weight. Even when low birth weight is not fatal it can cause a wide variety of health problems for the child, including retinopathy, intraventricular hemorrhage or necrotizing enterocolitis, among other more common chronic diseases such as diabetes and heart disease (8). The second important cause of infant mortality in the U.S. is birth defects. The third cause is Sudden Infant Death Syndrome (SIDS). SIDS refers to the sudden death of a seemingly healthy infant. SIDS differs from the other two primary causes in that its etiology is relatively unknown. While the cause of SIDS is still unknown, some risk factors have been identified. These include brain abnormalities, low birth weight, and sleeping position (sleeping on the stomach or side rather than the back) (9).

These three main causes of infant mortality vary in rate across the first year of life. Death due to low birth weight is more common within the first 4 months of life, while SIDS is more common in the last 4 months of the year. Birth defects tend to cause death in infants from right after the neonatal period up until the end of the first year of life (10).

Since the term congenital malformation encompasses a wide variety of diseases, infant mortality due to birth defects varies significantly across the spectrum of the defects

themselves (11). Anencephaly, a neural tube defect which results in parts of the infant's brain being missing, is fatal in all cases while other structural defects like cleft lip almost never result in mortality. Birth defects with the highest risk of mortality include anencephaly, encephalocele, trisomy 13 and 18, hypoplastic left heart syndrome, Ebstein's anomaly, common truncus, lung hypoplasia, esophageal atresia, renal hypoplasia and diaphragmatic hernia, among others (12). Prevention of birth defects is extremely difficult, as the causes are often multifactorial or unknown. However, one of the most strongly established methods of preventing neural tube defects involves folic acid supplementation. Folic acid has been shown to reduce the risk of neural tube defects significantly in multiple clinical trials, and in 1996 the FDA approved a rule for folic acid fortification in the U.S. grain supply (13). Since then, rates of neural tube defects in the U.S. have dropped sharply, and similar phenomena have been observed in other countries that have implemented fortification programs. Folic acid supplementation is one of the few established public health interventions that can prevent neural tube defects and the ensuing infant mortality.

Racial Trends

Health outcomes in the United States are inextricably linked to race. Due in large part to the systemic disenfranchisement of groups such as African-Americans, Hispanics, and American Indians, these outcomes tend to be worse for racial and ethnic minorities. Included in these health outcomes are those of maternal and child health, including infant mortality. Infant mortality rates are significantly higher for African-Americans, Hispanics, and American Indians when compared to Non-Hispanic Whites. Furthermore,

rates of infant mortality due to causes seen as preventable (i.e. low birth weight, some birth defects) have been shown to be higher in minority populations as well (6).

A large population based study conducted by Canfield et al. (2014) found significant differences in the prevalence of many of the 27 birth defects studied between minority races and the Non-Hispanic White baseline. American Indians in particular were at higher risk, with a significantly higher adjusted prevalence ratio in 16 of the 27 birth defects studied (14). Another large population cohort study from Egbe et al. (2015) showed that the prevalence of birth defects was actually lower for Hispanic (prevalence ratio=0.9) and Black (prevalence ratio=0.9) children than Non-Hispanic White and Asian children (2). However, since this study considered live births and not mortality it is possible that the results were skewed by more serious birth defects resulting in infants dying who could not later be counted. The reasons for these differences include access to prenatal care, maternal age and parity, supplement consumption, and environmental concerns. Hispanic mothers in particular are vulnerable to giving birth to children with neural tube defects due to dietary differences. Until 2015, the FDA had not approved folic acid supplementation for corn masa flour, a staple of Latin cuisine. Many Hispanic mothers miss this crucial supplementation without realizing it, resulting in higher rates of neural tube defects among Hispanic infants. The purpose of this analysis is to examine these racial trends in cause of infant mortality between the years 2010 and 2014, particularly the burden of birth defect-caused infant mortality, and how much or little these rates have changed since the original study published in 1990.

This analysis was performed in order to examine current racial disparities in birth defects associated infant mortality. This analysis is the first of its kind performed on the

U.S. birth cohort from 2010-2014, and explores whether or not recent birth defects related interventions have had a significant effect on gaps in proportional mortality. Since this analysis looked at the entire U.S. birth cohort, the Center for Disease Control and Prevention's National Vital Statistics System public linked birth-infant death data set for each of the five years was used.

METHODS

Information on live birth and death data was obtained from the National Vital Statistics System (NVSS) linked birth/death data set for the years 2010-2014. The data are collected and synthesized from state-linked birth/death certificate databases, and includes data from all fifty states along with Puerto Rico and Guam. Data from the period linked birth/death data set comes from state-linked files for the identification of linked birth and death certificates and National Center for Health Statistics (NCHS) natality and mortality computerized files. Each state links its own birth and death records for infants and share information with other states if the birth and death occur in different areas. These state-linked records were then combined into the NCHS data set. While most states have close to 100 percent of infant deaths linked to birth records by state, some states and territories were below the threshold necessary to prevent bias. Therefore a weight, given by the sum of the linked and unlinked infant deaths divided by the linked deaths, was added to the linked numerator file in order to account for states below the necessary threshold. Underlying cause of death, which is the most useful from a public health standpoint, is determined in a relatively standardized fashion across the U.S. based on the U.S. Standard Certificate, which in turn closely mirrors guidelines set by the World Health Organization. There were also many instances in which multiple causes of death were identified. In these cases, up to 20 ICD codes could be added to each case, but the most meaningful code, or the code recorded on the certificate as the primary cause of death, is given priority for analysis.

This analysis was restricted to live singleton births with reported birth weights born to U.S. residents. This information was available for 4,007,105 live births and

24,292 infant deaths in 2010, 3,959,529 live births and 23,723 infant deaths in 2011, 3,960,796 live births and 23,444 infant deaths in 2012, and 3,940,764 live births and 23,242 infant deaths in 2013, and 3,998,175 live births and 23,085 infant deaths in 2014. Infant race/ethnicity was classified based on mother's race/ethnicity. Maternal race and ethnicity was categorized into five broad groups: Non-Hispanic White, Non-Hispanic Black, Hispanic, Asian, and American Indian based on more specific racial categories. Infants with "unknown" or "other" listed for race were excluded from participation. Birth defects as conditions were defined according to the International Classification of Diseases (ICD) 10^{th} Edition. Any death caused by what the ICD called a birth defect was placed into the larger birth defects category. It was necessary to reclassify infants who had so-called "false" birth defects, or birth defects that resulted from low birth weight (defined as <2500 g at birth) in order to prevent a case from being classified both as due to low birth weight and due to birth defects. Since the 2014 data set changed the coding protocol for several variables, it was necessary to change the way race in particular was coded for this data, resulting in more missing values for this year than for previous years. Prevalence and proportional mortalities for each race were calculated for each year, along with stratified results based on birth weight and age at death. The Cochran-Armitage one-sided test for trend was also performed to analyze how infant mortality due to birth defects varied across the five year period for each category. The study was approved by the Emory University Human Subjects Research Committee, with a waiver for full review due to our use of aggregate, de-identified, public use data files. All data were analyzed using SAS v.9.3.

RESULTS

Results across Race/Ethnicity

Birth defects was the leading cause of infant mortality over this 5-year stretch (24,395 deaths, 20.71% of total) followed by low birth weight (21,108 deaths, 17.92% of total). The chi-square test demonstrated that there were significant differences between races in infant mortality due to birth defects across all five years (X^2=1591.71, p<0.0001). Compared to the Non-Hispanic White control group, the Non-Hispanic Black group had a markedly lower percentage of infants die because of birth defects across all five years (2010: 22.80% vs. 13.62%, 2011: 23.06% vs. 13.94%, 2012: 23.14% vs. 13.26%, 2013: 22.69% vs. 12.74%, 2014: 23.31% vs. 12.96%). This difference can at least partially be explained by low birth weight or gestational age at birth, which claims a much larger share of black infants than white infants. On the other hand, the Hispanic group had a higher percentage of infants die because of birth defects in all five years analyzed (2010: 22.80% vs. 25.96%, 2011: 23.06% vs. 26.35%, 2012: 23.14% vs. 26.71%, 2013: 22.69% vs. 25.89%, 2014: 23.31% vs. 24.40%). Overall, proportional mortality due to birth defects for the 5-year period was highest for Hispanics (25.86%) and Non-Hispanic whites (22.99%) and lowest for American Indians (20.40%) and Non-Hispanic Blacks (13.32%), with Asians in the middle (22.09%). The Cochran-Armitage test for trend showed a significant decrease in proportional mortality for Non-Hispanic Blacks (Z=1.88, p=0.0300) and Hispanics (Z=1.74, p=0.0407) over the 5-year period, with non-significant changes in the other three racial/ethnic groups (Non-Hispanic Whites: Z=-0.46, p=0.3244, American Indians: Z=1.40, p=0.0808, Asians: Z=-0.34,

p=0.3667), indicating that targeted interventions towards decreasing birth defects associated mortality within these two groups may have had some effect.

Results across Birth Weight Categories

Proportional mortality was further analyzed by birth weight categories (extremely low birth weight as <1000 grams, very low birth weight as between 1000 and 1500 grams, low birth weight as between 1500 and 2500 grams, and normal birth weight as greater than 2500 grams). Infant mortality due to birth defects was highest for all races within the very low and low birth weight categories (37.74% and 50.53% proportional mortality respectively) when compared to the extremely low and normal birth weight categories (6.04% and 25.47% proportional mortality respectively). Comparing proportional mortalities in birth weight categories among racial/ethnic groups revealed stark differences. Hispanics, who had the highest proportional birth-defects associated mortality, had the second lowest in the extremely low birth weight category (6.23% vs. 7.66% for Non-Hispanic Whites, 8.81% for American Indians, 7.08% for Asians, and 3.67% for Non-Hispanic Blacks). This unusually low proportion indicates that Hispanics as a group are more prone to deaths due to low birth weight or preterm birth than other racial/ethnic groups. Other birth weight categories bore out results similar to the overall proportional mortalities, with Hispanics having the highest proportional mortalities for the other three categories and Non-Hispanic Blacks having the lowest (see Tables 2a-2f). All but one of the tests for trend for the birth weight categories were not significant. The exception was the extremely low birth weight cohort, which displayed a significant decrease in proportional mortality across the 5-year period (Z=2.26, p=0.0118).

Results across Age at Death Categories

Proportional mortality was also analyzed by age at death categories (less than 1 hour, 1-24 hours, 1-7 days, 7-28 days, and 28-365 days). Mortality due to birth defects was highest among infants in the 1-7 day and 7-28 day cohorts (26.91% and 25.86% respectively). Racial differences in mortality remained consistent throughout each age cohort. Interestingly, Asians had the highest proportional mortality among all races in the 28-365 day group (25.46% vs. 13.48% for American Indians, 13.77% for Non-Hispanic Blacks, 18.03% for Non-Hispanic Whites and 24.03% for Hispanics). Other than this aberration, proportional mortality matched that of the overall results, with Hispanics having the highest proportion in the four other categories and Non-Hispanic Blacks having the lowest (see Tables 2a-2f). The test for trend showed a significant decrease only for the 1-24 hour group ($Z=1.92$, $p=0.0272$) and the 1-7 day group ($Z=2.76$, $p=0.0029$).

DISCUSSION

The infant mortality data from 2010-2014 retains many of the racial disparities in infant mortality due to birth defects that have plagued the U.S. for decades. Hispanics continue to have a higher proportion of infant mortality due to birth defects when compared to Non-Hispanic Whites. While Non-Hispanic Blacks do have a significantly lower proportion of infant mortality due to birth defects than any other race, this is in part due to massive disparities in mortality due to low birth weight and preterm birth, the causes of which have no adequate explanation other than maternal race. Congenital anomalies remain the main driver of infant mortality in the U.S., with low birth weight and preterm birth close behind.

While many of the racial disparities have not changed since the 1990 report, the numbers of the proportional mortalities are different now (10). The proportional mortality due to birth defects for Hispanics remains the highest among all racial/ethnic groups, and has increased from 24% to 25.86%. Proportional mortalities have had similar small changes for other racial groups, going from 18% to 20.40% for American Indians, 27% to 22.09% for Asians, 13% to 13.32% for Non-Hispanic Blacks, and 25% to 22.99% for Non-Hispanic Whites. Similar non-significant changes were observed when examining proportional mortalities stratified by both birth weight and age at death. Overall, infant mortality due to birth defects has not changed significantly in proportion, since the 1990 analysis was published. While it seems counterintuitive that proportional mortalities would increase for nearly every racial/ethnic group given improvements in medical technology and surveillance, there are a number of possible reasons for these changes. Improved treatment and prenatal care may have had a more significant effect on reducing

mortality due to low birth weight, which has more known causal factors and is seen as easier to prevent (11). The infant mortality rate has also decreased significantly for all racial/ethnic groups over the past few decades, meaning that even a relatively small decline in rates of birth defects associated mortality would still appear as an increase in proportion in this analysis.

The most recently published study to use the NVSS data set to examine racial differences in infant mortality due to birth defects was published in Pediatrics in 2012, and looked specifically at the effect of gestational age on these disparities (15). Since the specific focus of this study was gestational age, the neonatal and postneonatal categories were given more importance. This study found significantly lower rates of infant mortality due to birth defects among black neonates when compared to white neonates, which matches the trend found in this study. A possible explanation posited by the authors is that black infants, particularly those born with an extremely low birth weight and/or infants that die quickly after birth, are more likely to be classified in the fetal death category as opposed to the live birth and subsequent death category. In fact, the black fetal mortality rate is more than two times that of the white fetal mortality rate. This, along with the disproportionately high rate of black infants born preterm or with a low birth weight may explain their depressed proportional mortality due to birth defects. This study also demonstrated a significantly higher rate of infant mortality due to birth defects among Hispanics when compared to Non-Hispanic Whites, particularly in the neonatal period. The authors also conducted an analysis stratified on type of birth defects and found that Hispanics had higher rates of central nervous system defects and chromosomal abnormalities when compared to Non-Hispanic Whites. Overall, the results from the

previous study were similar to those of this analysis, indicating that racial differences in infant mortality due to birth defects have remained relatively constant over the past 10 years.

Strengths and Limitations

The main strength of this study is the massive sample size. The NVSS data set encompasses infant deaths from every U.S. state and territory, and contains reports from each state detailing what percentage of cases are accurately reported. The majority of states have 98% or more of death records linked with birth certificates for each year, meaning that the data itself is a robust representation of the U.S. birth cohort as a whole. The other main strength of the study is that the blueprint was in place. The 1990 study used the same NVSS data set and calculated, for the most part, the same statistics to analyze the data. These consistencies made for an easily replicable study, particularly with open access to an even more robust version of the same data sets used previously.

There were some limitations to this study. The first was that the full set of tables from the original 1990 study could not be recovered. Without these original tables it was impossible to do a full comparison of the results from that study to this one. While the main results related to proportional mortality among racial groups could be compared, specific details from some of the stratified analyses could not. Another limiting factor was the changes in the 2014 data set compared to the previous years. Several variables, including crucial variables related to race, were coded differently in the 2014 data set than the 2010-2013 data sets. The changes in these variables made it necessary to create a new more limited race variable to accurately compare the 2014 data to the data from the previous years. However, this new variable encompassed less of the total deaths in 2014 than the previous race variable did for the other years, resulting in a smaller sample for 2014. Additionally, this new race variable may have biased the results by excluding infants whose mothers had ambiguous ethnicities or infants who could not easily be fit

into one of the five broad racial categories used for analysis. While the sample was large enough to account for these biases, it makes the analysis of the 2014 data set less reliable than that of the previous 4 years.

Future Steps

There are still necessary steps to be taken to reduce racial disparities in infant mortality due to birth defects. Broadly, infant mortality due to birth defects can be reduced in two ways: by improving treatment options for children born with birth defects and by preventing birth defects from occurring by minimizing known risk factors, identifying and avoiding teratogens, and reduction of lifestyle factors that can contribute such as obesity or maternal smoking (16). The implementation of a fortification initiative that includes corn masa flour is a good first step to reducing these differences, particularly because Hispanics have had the highest proportional mortality for decades. The FDA did not approve the fortification of corn masa flour, a staple of the Latin American diet, until 2015, which could explain some of the continued difference in infant mortality due to birth defects between Hispanics and other racial groups. External factors such as air pollution and neighborhood acculturation have also been found to modify the risk of birth defects in immigrant Hispanic women (17). The test for trend indicated that infant mortality due to birth defects has reduced significantly both for Hispanics and Non-Hispanic Blacks over the 5-year period, which demonstrates the effectiveness of targeted interventions to reduce the prevalence of birth defects. Since the etiology of the majority of congenital anomalies is still unknown, further investigation into the biological basis of fatal birth defects is the next step to reducing their contribution to infant mortality beyond what has already occurred in the past 25 years. Prevention efforts are

also difficult because new potential teratogens are constantly being released into the environment without longitudinal studies validating their safety for mothers and infants. A bundled, multimodal approach involving both innovative prevention and treatment efforts is the only way to reduce both infant mortality due to birth defects and its racial disparities.

While proportional mortality due to birth defects have declined among all racial groups in the past 25 years, racial disparities remain. Further research and preventive measures are necessary to establish both reduction and equity of the burden of infant mortality due to birth defects.

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TABLES

Table 1a. Proportion of Infant Mortality due to Birth Defects, stratified by Race/Ethnicity, Age at Death, and Birth Weight, 2010

	Year 2010				
	Mortality Due to Birth Defects (n, %)		Mortality Due to all other causes (n, %)		p-value (Chi square)
Total deaths	5055	20.81%	19237	79.19%	
Age at death					
<1 hour	591	16.39%	3014	83.61%	<0.0001
1-24 hours	1329	21.40%	4881	78.60%	
1-7 days	825	28.40%	2080	71.60%	
7-28 days	834	25.43%	2445	74.57%	
28-365 days	1476	17.80%	6817	82.20%	
Race/Ethnicity					
NH White	2526	22.80%	8554	77.20%	<0.0001
NH Black	912	13.62%	5782	86.38%	
Hispanic	1267	25.96%	3614	74.04%	
American Indian	82	24.19%	257	75.81%	
Asian	216	22.29%	753	77.71%	
Birth Weight					
< 1000 g	729	6.57%	10360	93.43%	<0.0001
1000-1500 g	583	37.71%	963	62.29%	
1500-2500 g	1760	49.47%	1798	50.53%	
>2500 g	1981	25.59%	5759	74.41%	

Table 1b. Proportion of Infant Mortality due to Birth Defects, stratified by Race/Ethnicity, Age at Death, and Birth Weight, 2011

	Year 2011				
	Mortality Due to Birth Defects (n, %)		Mortality Due to all other causes (n, %)		p-value (Chi square)
Total deaths	4961	20.91%	18762	79.09%	
Age at death					
<1 hour	592	16.24%	3054	83.76%	<0.0001
1-24 hours	1301	21.20%	4836	78.80%	
1-7 days	796	26.72%	2183	73.28%	
7-28 days	836	27.04%	2256	72.96%	
28-365 days	1436	18.25%	6433	81.75%	
Race/Ethnicity					
NH White	2487	23.06%	8298	76.94%	<0.0001
NH Black	921	13.94%	5688	86.06%	
Hispanic	1223	26.35%	3418	73.65%	
American Indian	58	17.63%	271	82.37%	
Asian	211	21.33%	778	78.67%	
Birth Weight					
< 1000 g	682	6.16%	10394	93.84%	<0.0001
1000-1500 g	562	37.24%	947	62.76%	
1500-2500 g	1788	50.84%	1729	49.16%	
>2500 g	1922	25.70%	5557	74.30%	

Table 1c. Proportion of Infant Mortality due to Birth Defects, stratified by Race/Ethnicity, Age at Death, and Birth Weight, 2012

	Year 2012				
	Mortality Due to Birth Defects (n, %)		Mortality Due to all other causes (n, %)		p-value (Chi square)
Total deaths	4920	20.99%	18524	79.01%	
Age at death					
<1 hour	590	17.14%	2852	82.86%	<0.0001
1-24 hours	1258	20.05%	5016	79.95%	
1-7 days	866	28.51%	2171	71.49%	
7-28 days	806	27.16%	2162	72.84%	
28-365 days	1400	18.13%	6323	81.87%	
Race/Ethnicity					
NH White	2470	23.14%	8206	76.86%	<0.0001
NH Black	858	13.26%	5614	86.74%	
Hispanic	1224	26.71%	3359	73.29%	
American Indian	76	22.42%	263	77.58%	
Asian	225	22.19%	789	77.81%	
Birth Weight					
< 1000 g	647	5.90%	10310	94.10%	<0.0001
1000-1500 g	556	39.91%	837	60.09%	
1500-2500 g	1796	51.28%	1706	48.72%	
>2500 g	1915	25.67%	5546	74.33%	

Table 1d. Proportion of Infant Mortality due to Birth Defects, stratified by Race/Ethnicity, Age at Death, and Birth Weight, 2013

	Year 2013				
	Mortality Due to Birth Defects (n, %)		Mortality Due to all other causes (n, %)		p-value (Chi square)
Total deaths	4735	20.37%	18507	79.63%	
Age at death					
<1 hour	561	15.64%	3027	84.36%	<0.0001
1-24 hours	1265	20.63%	4866	79.37%	
1-7 days	768	25.48%	2246	74.52%	
7-28 days	751	25.22%	2227	74.78%	
28-365 days	1390	18.46%	6141	81.54%	
Race/Ethnicity					
NH White	2425	22.69%	8264	77.31%	<0.0001
NH Black	820	12.74%	5618	87.26%	
Hispanic	1151	25.89%	3294	74.11%	
American Indian	53	17.91%	243	82.09%	
Asian	214	22.02%	758	77.98%	
Birth Weight					
< 1000 g	622	5.72%	10253	94.28%	<0.0001
1000-1500 g	517	36.56%	897	63.44%	
1500-2500 g	1725	49.91%	1731	50.09%	
>2500 g	1866	25.35%	5494	74.65%	

Table 1e. Proportion of Infant Mortality due to Birth Defects, stratified by Race/Ethnicity, Age at Death, and Birth Weight, 2014

	Year 2014				
	Mortality Due to Birth Defects (n, %)		Mortality Due to all other causes (n, %)		p-value (Chi square)
Total deaths	4724	20.46%	18361	79.54%	
Age at death					
<1 hour	585	17.11%	2834	82.89%	<0.0001
1-24 hours	1272	20.12%	5049	79.88%	
1-7 days	746	25.44%	2186	74.56%	
7-28 days	723	24.44%	2235	75.56%	
28-365 days	1398	18.75%	6057	81.25%	
Race/Ethnicity					
NH White	2132	23.31%	7014	76.69%	<0.0001
NH Black	703	12.96%	4722	87.04%	
Hispanic	1122	24.40%	3477	75.60%	
American Indian	44	19.05%	187	80.95%	
Asian	188	22.73%	639	77.27%	
Birth Weight					
< 1000 g	633	5.83%	10220	94.17%	<0.0001
1000-1500 g	539	37.33%	905	62.67%	
1500-2500 g	1717	51.18%	1638	48.82%	
>2500 g	1831	25.04%	5480	74.96%	

Table 1f. Proportion of Infant Mortality due to Birth Defects, stratified by Race/Ethnicity, Age at Death, and Birth Weight, 2010-2014

	Years 2010-2014					
	Mortality Due to Birth Defects (n, %)		Mortality Due to all other causes (n, %)		p-value (Chi square)	p-value (Cochran-Armitage one sided)
Total deaths	24395	20.71%	93391	79.29%		
Age at death						
<1 hour	2919	16.49%	14781	83.51%	<0.0001	0.3445
1-24 hours	6425	20.68%	24648	79.32%		0.0272
1-7 days	4001	26.91%	10866	73.09%		0.0029
7-28 days	3950	25.86%	11325	74.14%		0.0740
28-365 days	7100	18.27%	31771	81.73%		0.0625
Race/Ethnicity						
NH White	12040	22.99%	40336	77.01%	<0.0001	0.3244
NH Black	4214	13.32%	27424	86.68%		0.0300
Hispanic	5987	25.86%	17162	74.14%		0.0407
American Indian	313	20.40%	1221	79.60%		0.0808
Asian	1054	22.09%	3717	77.91%		0.3667
Birth Weight						
< 1000 g	3313	6.04%	51537	93.96%	<0.0001	0.0118
1000-1500 g	2757	37.74%	4549	62.26%		0.3665
1500-2500 g	8786	50.53%	8602	49.47%		0.1749
>2500 g	9515	25.47%	27836	74.53%		0.1847

Table 2a. Proportional Mortality due to Birth Defects for Age at Death and Birth Weight categories, stratified by Race/Ethnic Group, 2010

	Race/Ethnicity				
	NH White	NH Black	Hispanic	American Indian	Asian
Age at Death					
<1 hour	20.54%	7.99%	18.94%	35.29%	14.69%
1-24 hours	26.91%	11.84%	25.18%	25.35%	20.78%
1-7 days	28.55%	22.30%	33.83%	36.00%	26.12%
7-28 days	26.43%	18.51%	32.71%	23.81%	25.62%
28-365 days	17.38%	13.40%	23.82%	19.76%	25.18%
Birth Weight					
<1000 g	8.36%	4.09%	6.21%	9.80%	7.39%
1000-1500 g	35.63%	33.16%	47.72%	60.00%	25.00%
1500-2500 g	51.29%	37.05%	58.50%	50.00%	51.43%
>2500 g	24.26%	19.64%	34.37%	20.96%	35.25%

Table 2b. Proportional Mortality due to Birth Defects for Age at Death and Birth Weight categories, stratified by Race/Ethnic Group, 2011

	Race/Ethnicity				
	NH White	NH Black	Hispanic	American Indian	Asian
Age at Death					
<1 hour	19.56%	11.21%	17.29%	18.18%	14.56%
1-24 hours	27.97%	10.83%	24.00%	29.51%	17.11%
1-7 days	26.41%	19.59%	34.65%	39.47%	23.38%
7-28 days	27.54%	19.29%	34.88%	16.22%	33.06%
28-365 days	18.08%	14.28%	25.40%	7.38%	22.76%
Birth Weight					
<1000 g	8.25%	3.84%	5.69%	10.00%	6.22%
1000-1500 g	37.37%	30.36%	46.01%	25.00%	32.26%
1500-2500 g	50.38%	41.54%	62.77%	45.10%	51.25%
>2500 g	25.06%	20.06%	35.24%	13.66%	28.42%

Table 2c. Proportional Mortality due to Birth Defects for Age at Death and Birth Weight categories, stratified by Race/Ethnic Group, 2012

	Race/Ethnicity				
	NH White	NH Black	Hispanic	American Indian	Asian
Age at Death					
<1 hour	20.97%	8.49%	18.43%	32.56%	19.33%
1-24 hours	25.95%	10.13%	23.23%	30.00%	18.52%
1-7 days	29.27%	18.68%	38.44%	20.59%	25.00%
7-28 days	28.68%	19.85%	34.37%	21.43%	23.84%
28-365 days	17.51%	13.89%	25.16%	16.67%	24.75%
Birth Weight					
<1000 g	7.50%	3.42%	6.44%	7.48%	7.26%
1000-1500 g	43.23%	27.81%	45.58%	21.05%	44.44%
1500-2500 g	53.27%	40.29%	58.70%	55.36%	50.00%
>2500 g	24.27%	19.26%	36.98%	21.15%	26.95%

Table 2d. Proportional Mortality due to Birth Defects for Age at Death and Birth Weight categories, stratified by Race/Ethnic Group, 2013

	Race/Ethnicity				
	NH White	NH Black	Hispanic	American Indian	Asian
Age at Death					
<1 hour	19.04%	7.55%	18.66%	20.00%	17.83%
1-24 hours	27.07%	10.74%	23.84%	24.49%	14.60%
1-7 days	25.97%	18.84%	31.37%	33.33%	28.29%
7-28 days	26.44%	17.58%	31.32%	26.32%	25.62%
28-365 days	18.35%	12.98%	26.72%	9.22%	26.87%
Birth Weight					
<1000 g	6.98%	3.21%	6.59%	9.18%	8.30%
1000-1500 g	39.36%	26.54%	44.11%	31.58%	32.31%
1500-2500 g	51.33%	36.40%	60.38%	43.59%	54.94%
>2500 g	24.77%	20.01%	34.50%	15.22%	25.51%

Table 2e. Proportional Mortality due to Birth Defects for Age at Death and Birth Weight categories, stratified by Race/Ethnic Group, 2014

	Race/Ethnicity				
	NH White	NH Black	Hispanic	American Indian	Asian
Age at Death					
<1 hour	22.66%	8.42%	18.36%	17.65%	11.89%
1-24 hours	25.73%	10.29%	24.71%	33.33%	17.00%
1-7 days	25.79%	17.21%	35.28%	25.00%	25.86%
7-28 days	24.94%	18.43%	31.01%	14.71%	34.51%
28-365 days	19.22%	14.66%	19.93%	13.27%	28.85%
Birth Weight					
<1000 g	7.10%	3.81%	6.25%	7.14%	6.05%
1000-1500 g	41.78%	31.93%	34.67%	23.08%	43.48%
1500-2500 g	54.76%	41.26%	57.53%	53.85%	50.41%
>2500 g	25.97%	21.52%	32.00%	14.15%	32.87%

Table 2f. Proportional Mortality due to Birth Defects for Age at Death and Birth Weight categories, stratified by Race/Ethnic Group, 2010-2014

	Race/Ethnicity				
	NH White	NH Black	Hispanic	American Indian	Asian
Age at Death					
<1 hour	20.51%	8.78%	18.33%	24.74%	15.67%
1-24 hours	26.73%	10.76%	24.19%	28.38%	17.57%
1-7 days	27.21%	19.29%	34.79%	31.33%	25.71%
7-28 days	26.84%	18.74%	32.87%	20.73%	28.25%
28-365 days	18.03%	13.77%	24.10%	13.48%	25.46%
Birth Weight					
<1000 g	7.66%	3.67%	6.23%	8.81%	7.08%
1000-1500 g	39.34%	29.94%	43.70%	33.73%	35.98%
1500-2500 g	52.11%	39.20%	59.56%	49.79%	51.68%
>2500 g	24.81%	20.00%	34.60%	17.31%	29.57%

Figure 1. Proportion of Mortality due to Birth Defects, Clustered by Race/Ethnicity