

Delaware Infant Mortality

David A. Paul, MD;¹ Neal D. Goldstein, PhD, MBI;² Robert Locke, DO, MPH³

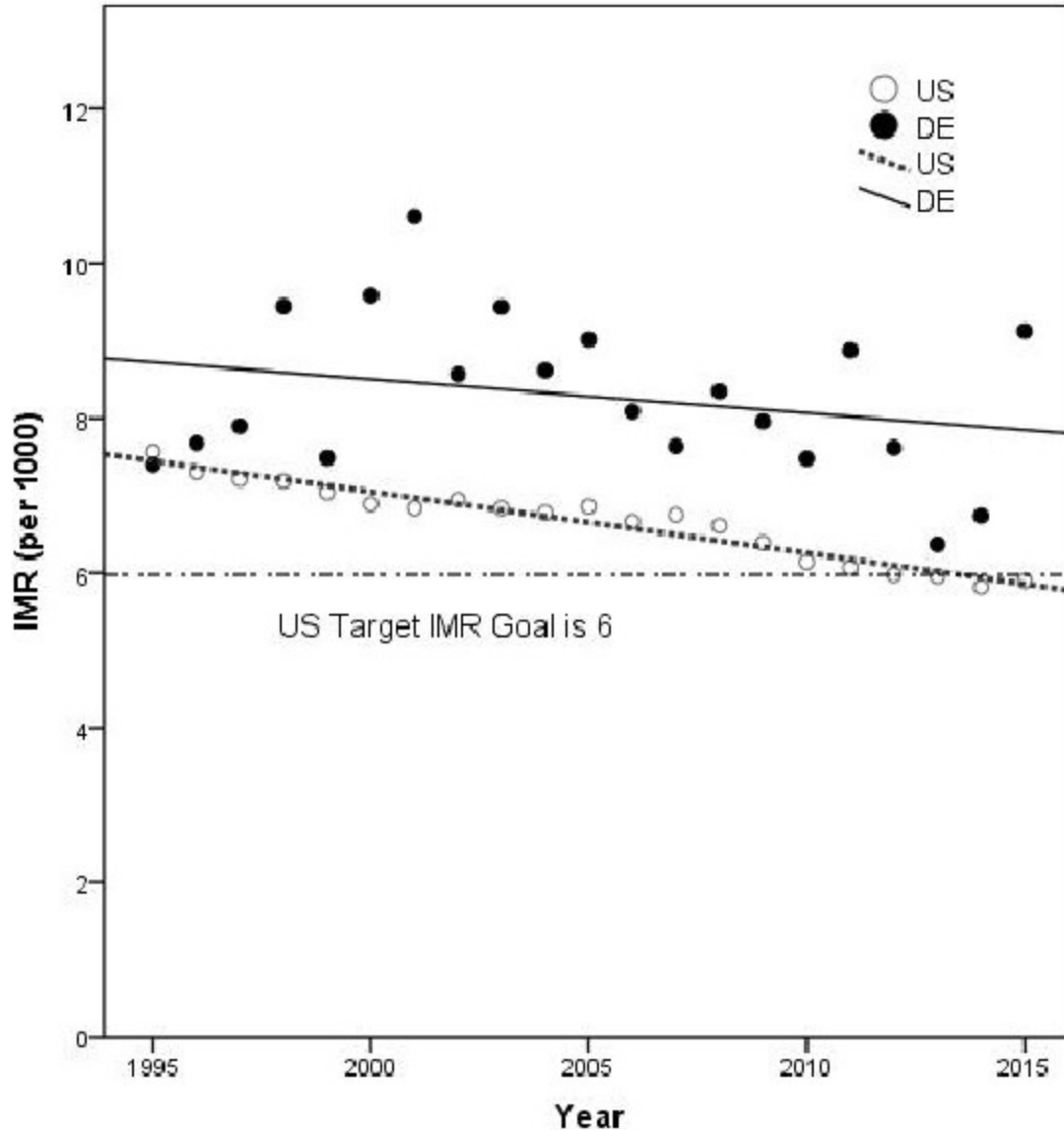
1. Clinical Leader, Women and Children's Service Line; Chair, Pediatrics, Christiana Care Health System; Professor, Pediatrics, Sidney Kimmel Medical College, Thomas Jefferson University; Governor Appointed Chair, Delaware Healthy Mother and Infant Consortium

2. Infectious Disease Epidemiologist, Christiana Care Health System; Assistant Research Professor, Department of Epidemiology & Biostatistics, Drexel University Dornsife School of Public Health

3. Attending Critical Care Neonatologist, Christiana Care Health System; Professor, Pediatrics, Sidney Kimmel Medical College, Thomas Jefferson University

Delaware's infant mortality rate remains above Healthy People 2020 targeted goal of 6.0 per 1000 births (Figure 1).^{1,2} The structural issues that underline the Delaware's elevated rate require a forward-thinking public health approach. This commentary and review will describe the underlying factors contributing to Delaware's infant mortality rate (IMR), and the Delaware State Governmental, State Health Systems and public health entities current approaches and challenges to improve outcomes.

Figure 1. US and Delaware Infant Mortality Rate and US Healthy 2020 Target Goals (Best fit lines)

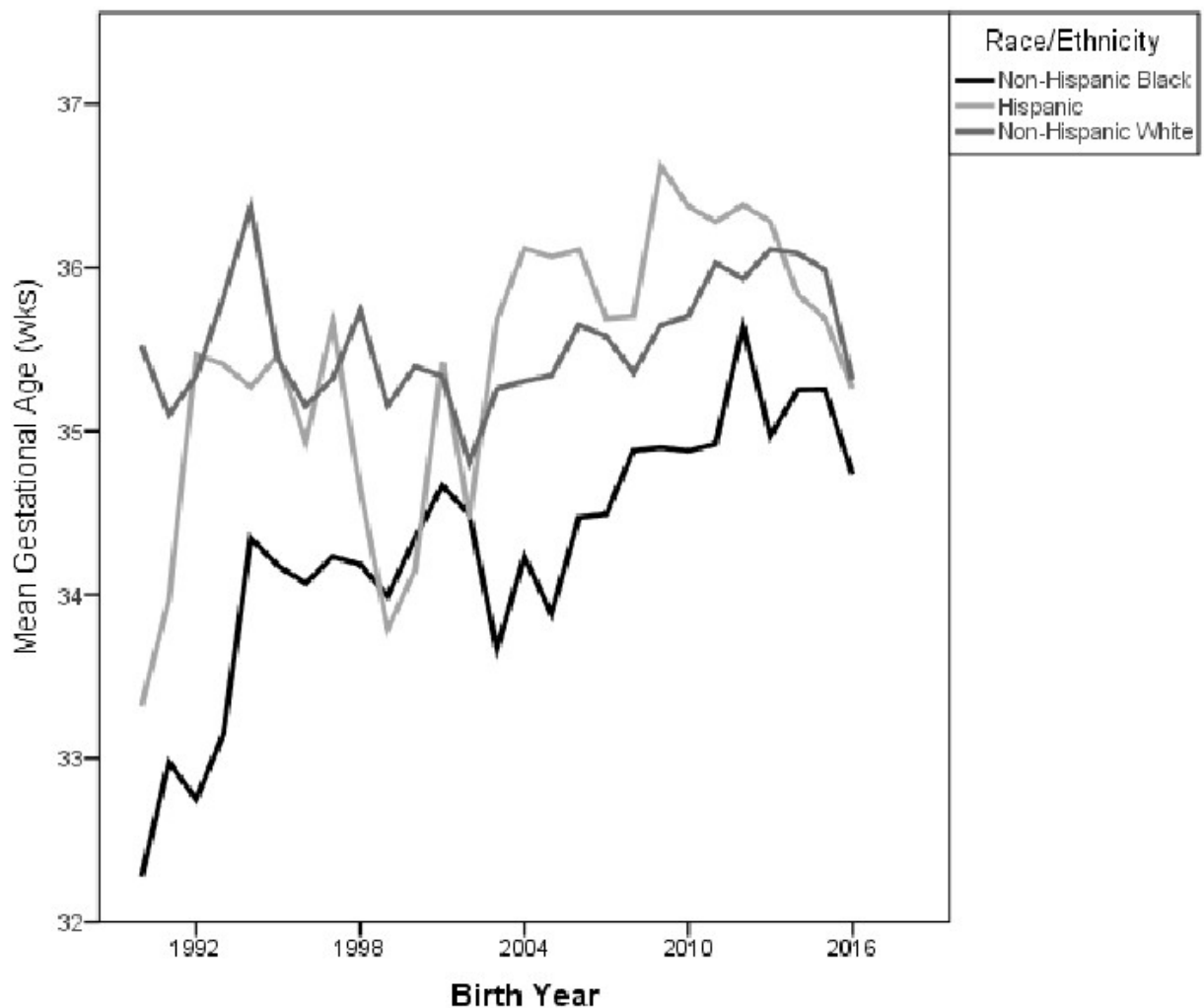


Infant mortality is divided into early (0-28 days or neonatal mortality) and late (29 – 364 days or post- neonatal mortality). National and local major factors contributing to neonatal mortality include preterm birth, birth defects, health disparities and underlying maternal health complications causing preterm delivery or birth related compromise (Table 1).³⁻⁸ These factors are interrelated. Health disparities, especially those delineated across racial/ethnic divisions, are associated with differential rates of prematurity. Infants with congenital malformations are more likely to be delivered prematurely. Poor glucose control is major teratogen.⁹ Women with diabetes, weight-related and/or hypertensive disorders are more likely to deliver preterm or an infant with complications.⁶ Health disparities, socio-economic and race-ethnicity, exacerbates these maternal health issues.^{3,8,10} Racial differences in prematurity rates, especially elevated Black rates of premature birth, is a major factor for the underlying racial differences in infant mortality and utilization of high cost services such as the NICU (Figure 2).^{2,3}

Table 1. Leading Causes of Infant Mortality

Neonatal < 28 days	Post-neonatal 28-364 days
67% of Infants Deaths	33% of Infant Deaths
Leading Causes: Prematurity Birth Defects Maternal health conditions Lack of Access to Risk-Appropriate Care Intrapartum birth/delivery complications	Leading Causes: Inappropriate Sleep Position; Sudden Unexpected infant death (SUID); Sudden infant death syndrome (SIDS); Congenital Malformations Injury Infection

Figure 2. Racial-Ethnic Differences in Gestational Age Among Infants Admitted to the Christiana Care Health System NICU Over Time



Post-neonatal infant mortality is most commonly associated with improper sleep related position, sudden unexpected infant death or sudden infant death syndrome (SIDS), injury and infant infection.^{11,12} Similar to neonatal mortality, all of these leading causes have a multifactorial health disparity component that includes individual and contextual aspects.

These interactions are not unique to Delaware. A proportion of Delaware's infant mortality rate compared to other states reflects demographic differences with a higher population of groups in Delaware associated with preterm delivery. However, demographic variables do not account for all of the differences in Delaware infant mortality. Correcting for maternal Black/White/Hispanic race-ethnicity, tobacco use, and cesarean section rates, there remains excess mortality and prematurity in the state.^{5,13-15} Based upon information from the Delaware's Birth Defect Registry, this does not appear to arise from excess congenital malformations.¹⁶ More likely, the primary driving cause is from the other contributing factors, including higher rates of preterm births compared to similar population states (Figure 3; Table 2).

Figure 3. Percent preterm births in DE and US 1999-2015. (Note: Beginning in 2014 NCHS changed the standard for gestational period from the Last Menstrual Period based gestation period to the Obstetric/Clinical Gestation Estimate based gestation period)

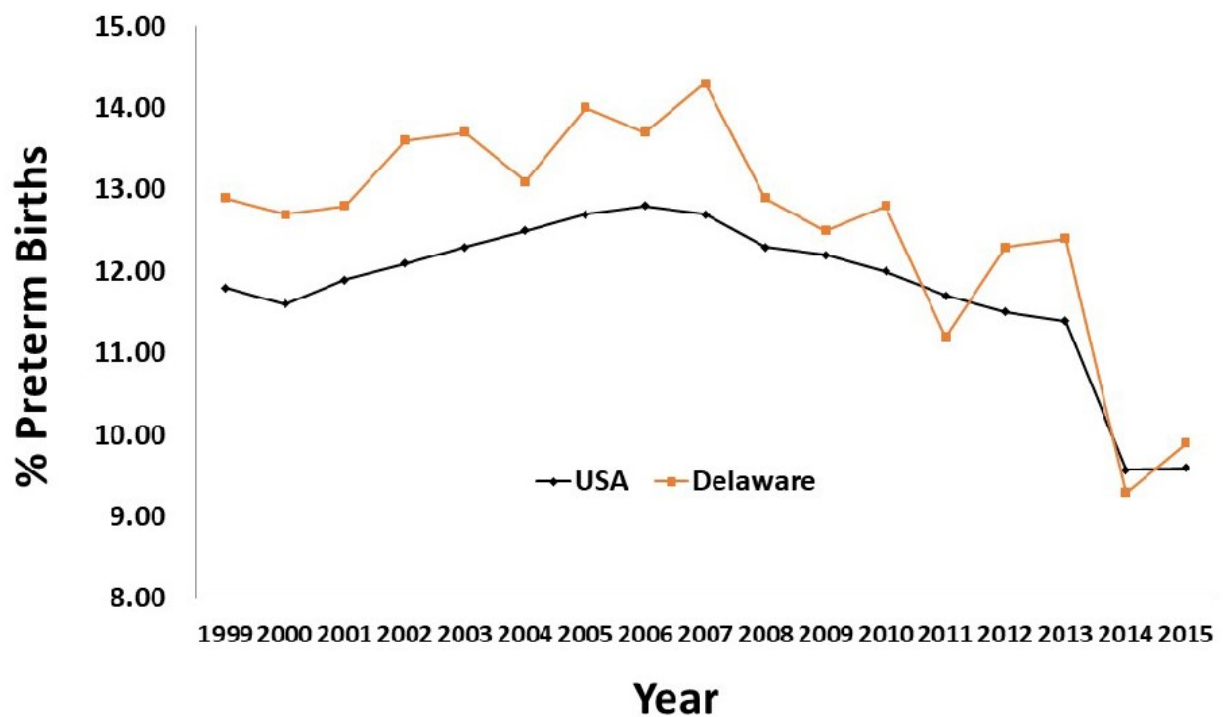


Table 2. Preterm births < 1500 grams and total births in year 2015 among similar birth population states

State	Preterm Births < 1500 grams	Percent Preterm Births < 1500 gms	Total Births
Delaware	208	1.87%	11,116
Alaska	105	0.93%	11,282
Montana	104	0.83%	12,583
Rhode Island	155	1.41%	10,933
South Dakota	127	1.03%	12,336

A primary driver of infant mortality within Delaware is the elevated rate of prematurity.^{2,11} The risk of infant death is inversely related to gestational age. Even small changes in gestational age

can have a significant impact. Nationally there has been a successful effort to reduce elective deliveries prior to 39 weeks. Although 37 weeks may be perceived to be “term” by conventional and older classification systems, 37-38 weeks deliveries have a high relative risk of physiologic compromise and poor outcomes compared to 39-40 weeks gestation.¹⁷ Eliminating elective deliveries prior to 39 weeks have had a meaningful impact. The March of Dimes, physician groups, governmental entities and local maternity centers deserve significant credit in converting this evidence-based goal into every day practice reality. The greatest risk of death is in the smallest infants. Although the number of infants born <1000 grams (2.2 pounds) is less than 1%, this group of infants accounts for over 50% of the Delaware’s IMR (Figure 4A and 4B).^{2,15}

Figure 4A: Percentage of Delaware Infant deaths by birthweight (bars) compared to percentage of births by weight (line).

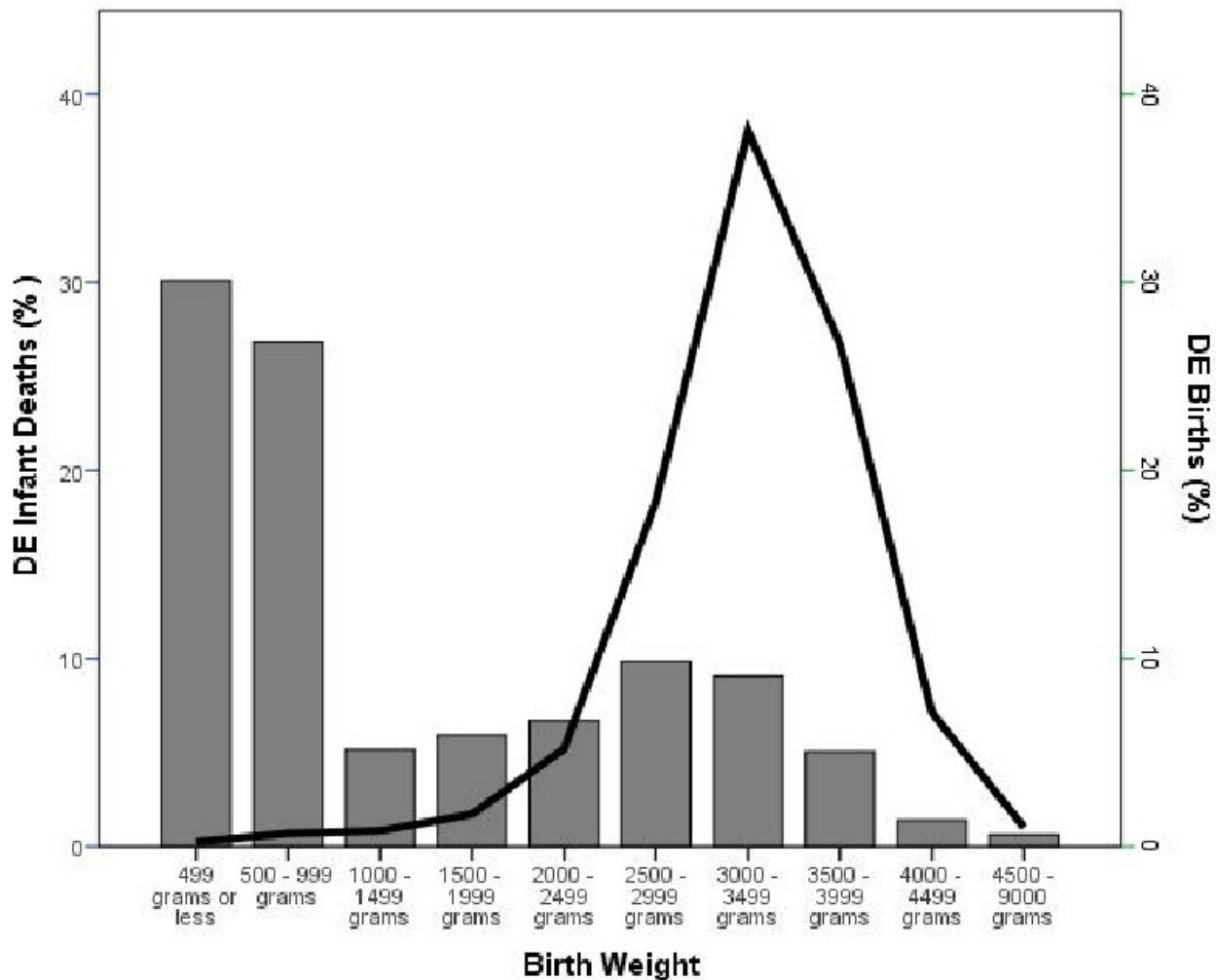
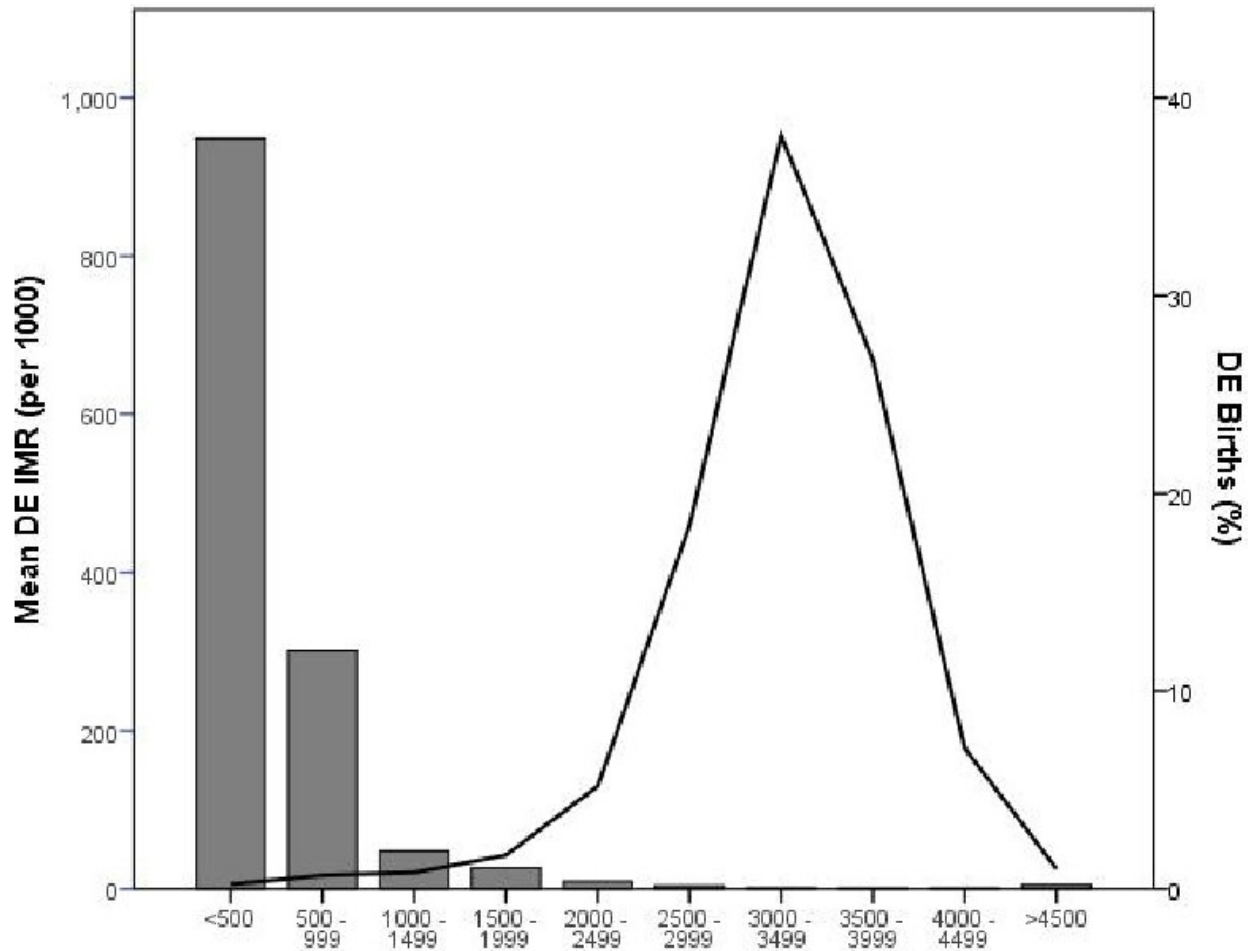


Figure 4B: Delaware IMR by birthweight (bars) compared to percentage of births by weight (lines).



There are limited medical interventions that can reduce the rate of prematurity.¹⁸ Tocolytic medications to stop preterm labor have limited efficacy. Purposefully limiting the number of multiple gestation pregnancies, especially beyond twins in cases of infertility and following nationally recognized guidelines is one effective intervention but of limited scope. At a population level, prevention of a subsequent preterm birth delivery can be slightly altered by 17-OH progesterone.

Access to prenatal care remains high in Delaware.² An additional important factor is spacing of pregnancies. An interpregnancy interval <18 months is a risk for a preterm delivery.¹⁹⁻²¹ Interpregnancy interval is partially under the domain of an individual, but the opportunity to have access to affordable and effective contraceptives is primarily determined by federal and state policies.

Teenage births across Delaware have markedly declined in the past 10 years through a combination of national trends and local efforts.²² A reduction in elective multiple births, especially multiples beyond twins, have also diminished.^{9,11,15} The occurrence of preterm triplets and quadruplets because of infertility interventions is now an uncommon event in Delaware.

Regionalization of care through coordination of transport and perinatal services can reduce infant mortality.²³

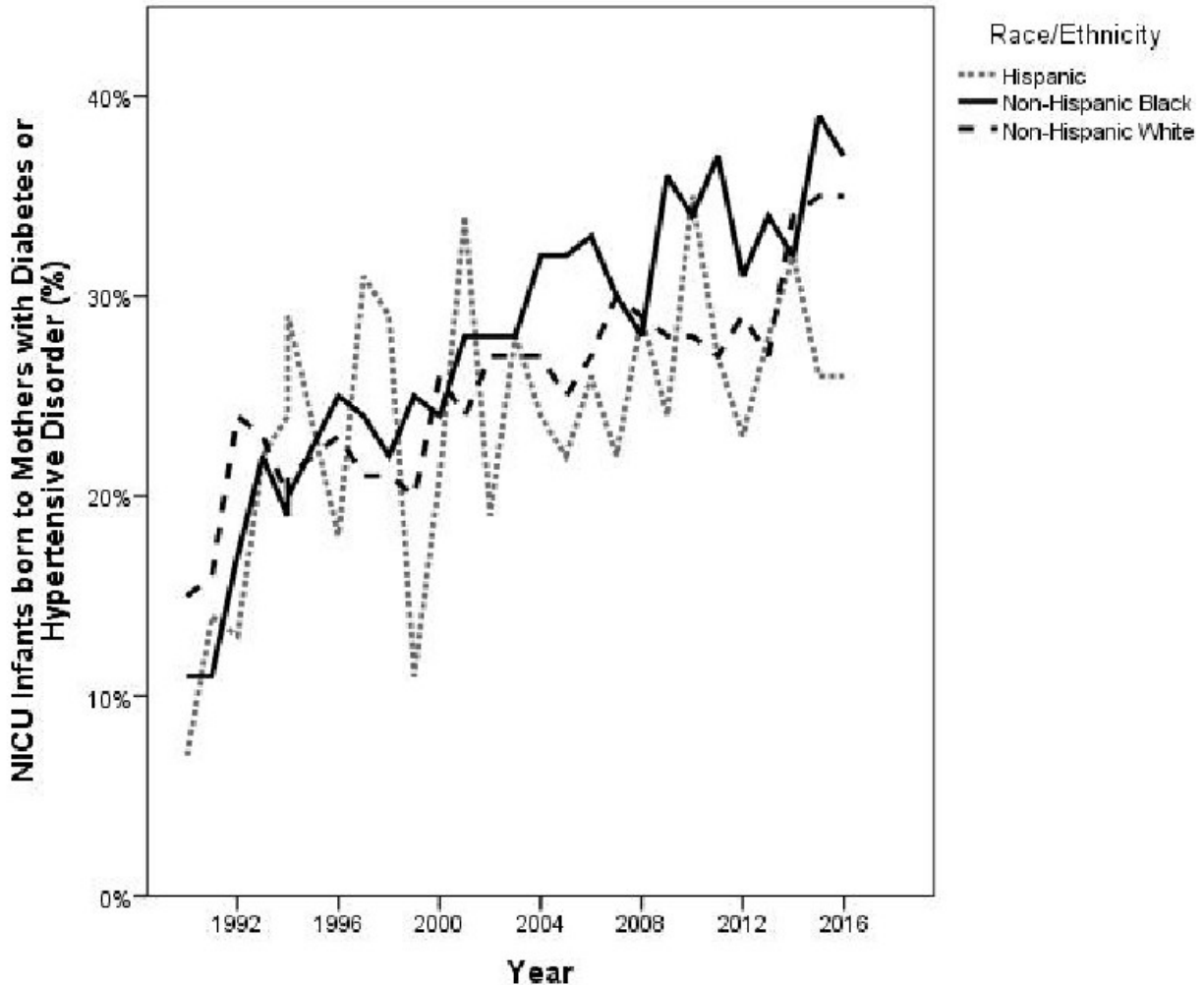
Within Delaware there is verbally agreed upon non-binding agreement to follow best practice national guidelines that the highest risk infants and infants with congenital malformations deliver at Delaware's regional perinatal center. With rare exceptions, these national best practices are generally followed. There is an opportunity to further coordinate maternal and infant transports and levels of care as designated by the AAP and ACOG. Although many of the drivers for preterm delivery occur outside the hospital, benchmarking health system and health provider outcomes are essential steps in understanding provider and hospital system opportunities for improvement.

Once an infant is born prematurely, especially for those <1500 grams, survival rates in Delaware are equivalent to or exceed expected rates compared to European or other US states.^{24,25} Christiana Care Health System (CCHS), the largest and only Level III NICU in the state at a delivery hospital, is the primary provider for infants <1500 grams birthweight. CCHS NICU, meets or exceeds all risk-adjusted outcomes measures for infants < 1500 grams birthweight among comparative databases, including the largest international benchmarking quality database, the Vermont-Oxford Network, with over 1000 US and international neonatal intensive care units.²⁴ These outcomes reflect a high-volume, high-capacity system of maternal and infant care providers and a health system that has made this component of care a priority.

Delaware's children's hospital, Nemours/A.I. duPont Hospital for Children, participates in selective benchmarking. Nemours cardiothoracic program has equivalent outcomes to the best program in Pittsburgh and Philadelphia.²⁶ Various subspecialty surgical programs meet or exceed comparative outcomes.²⁷ Nemours Extracorporeal Membrane Oxygenation (ECMO) team are leaders among the benchmarking ELSO registry.²⁸ The Nemours NICU does not participate in the Vermont Oxford or other large medical outcome comparative networks for premature infants at their Delaware site. All of the Delaware maternal delivery centers are Baby Friendly USA certified, a rigorous program to promote breastfeeding, except for St. Francis and Nanticoke Hospitals.²⁹ Christiana Care Health System Neonatology, Christiana Maternal Fetal Medicine teams and members of Nemours are in leadership positions in national quality improvement efforts and national organizations that set standards of care.

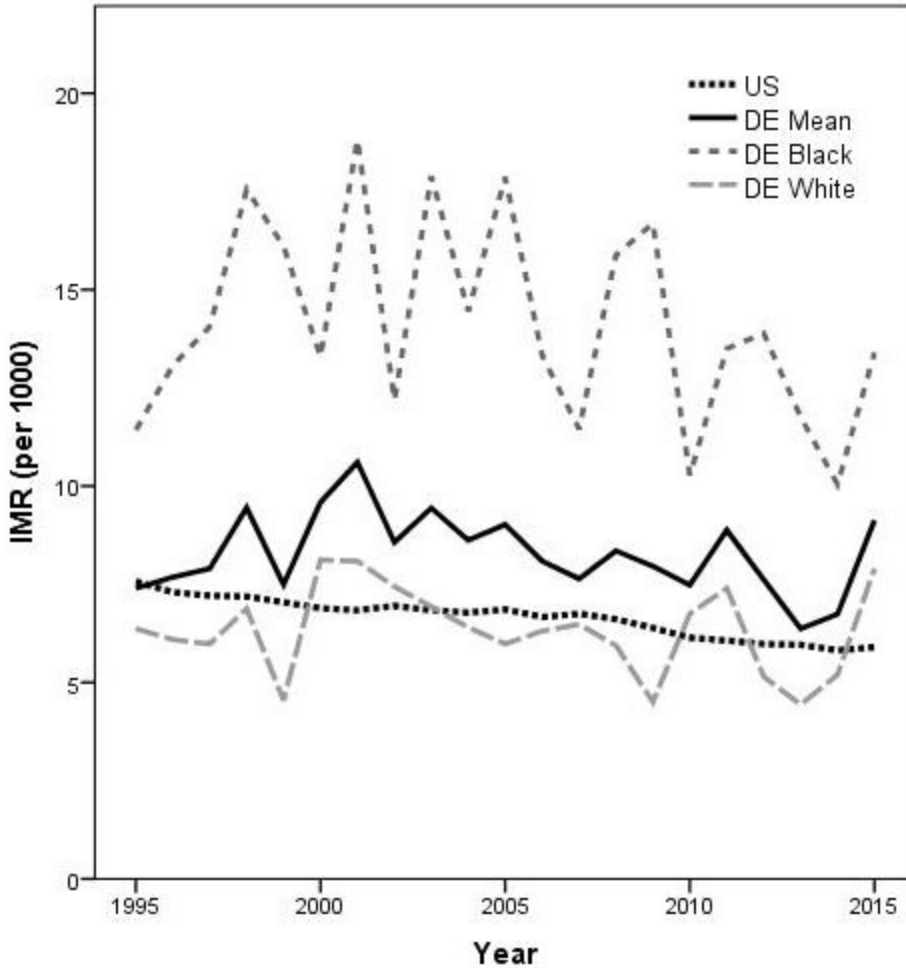
If the within-hospital risk-adjusted care in Delaware meets or exceeds national and international benchmarks, why is DE's infant mortality elevated? All research indicates that the greater than expected mortality rate comes from a disproportionate rate of high risk infants being born to high risk mothers.^{5,6,13-15,30} Previously our group demonstrated that the degree of physiologic compromise of infants being born continues to rise.^{13,14} Though recently improving, the rate of premature infants in Delaware has been nearly twice that of similar population states.² On the positive side, Delaware's teen pregnancy rate has been declining.^{2,16} In contrast, maternal preconception, intra- and inter-conception health, especially with respect to hypertensive and weight-related disorders, continues to have an untoward impact on adverse neonatal outcomes (Figure 5).¹⁵ Of crucial importance, there remain significant health disparities in outcomes. Our group has demonstrated that there are complex interactions between race/ ethnicity, maternal obesity, hypertensive disorders, placental factors, and adverse neonatal outcomes in including death and/or chronic lung injury among survivors.^{6,7,14,30} These have been detailed in our other previous publications.

Figure 5: Percent of infants admitted to the Christiana Hospital NICU whose mothers had pre-existing or gestational diabetes or a hypertensive disorder during pregnancy.



From a public health perspective, addressing health disparities and underlying maternal intra- and preconception health are potentially modifiable factors that the state of Delaware, citizens, health systems, faith-based groups and non-profits can make a significant impact. There is a wide infant mortality gap between non-Hispanic Black and non-Hispanic White infants. The DE non-Hispanic White IMR is statistically similar to the US national IMR, while the DE non-Hispanic Black IMR is frequently twice as high (Figure 6).² The difference is not based upon modifiable behaviors, such as tobacco use, education or socio-economic status.

Figure 6. Comparative Infant Mortality Rates Between US and Delaware Based on Race/Ethnicity



Non-Hispanic Blacks use tobacco less frequently than non-Hispanic Whites while pregnant, yet the IMR for Black non-smokers is higher than White smokers during pregnancy.³¹ Nor is this education or economic based. The IMR is higher among non-Hispanic Blacks whose mother has a college degree compared to non-Hispanic Whites without a high school diploma.² Nationally, Blacks have double the IMR of Hispanics despite a similar socio-economic status.² Nationally there is an increased rate of black premature infant death. At Christiana Care Health System there is not an elevated risk of death prior to hospital discharge compared to other racial/ethnicities. The hospital birth survival rate at Christiana Care Health System for ≤ 30 week premature Black infants is better than Whites (Table 3).¹⁵ There is no difference between non-Hispanic White or Hispanics in <30 week prematurity hospital survival, suggesting that there is no adverse healthcare bias or survival based on race/ethnicity.¹⁵

Table 3. Christiana Care Health System pre-hospital discharge mortality differences based upon race/ethnicity controlling for birth gestational age and birth year

Pre-Hospital Discharge Mortality Birth Gestational Age ≤ 30 weeks		P	OR	95% Confidence Interval	
				Lower	Upper
Race/Ethnicity	Hispanic	.141	.720	.465	1.115
	Non-Hispanic Black	.001	.691	.552	.863

	Non-Hispanic White	.	1	.	.
a. Controlling for Year of Birth and Birth Gestational Age					

In European countries, racial differences in outcomes are less apparent. Non-Hispanic Blacks born in Europe have the same IMR as non-Hispanic Whites. Recent African-American immigrants to the United States have the same birthweight and infant outcomes as US Whites.^{32,33} Within two generations the Black-White gap appears. Epigenetics may play an important role.³⁴⁻³⁶ The US Black vs White IMR difference is present only in Black Americans who have been here for more than one generation. This evidence suggests that there are important non-genetic, social factors influencing the Black population in the US compared to other countries, consistent with the “Weathering Hypothesis” that has an untoward risk for a poor pregnancy outcome.^{37,38}

Blacks experiencing racism are 2.7 times as likely to deliver an infant <1500 grams.³² Chronic stress and cumulative life experiences are risks for delivering preterm and a low birthweight infant.^{37,39} These known physiologic responses during pregnancy are mimicked in animal models and present in large epidemiologic observations. These experiences lead to prenatal programming in which the experiences of women, starting in utero and early childhood, can alter the risk for an adverse pregnancy outcome, cross generations and may take generations to repair. These prenatal programming effects are beyond chronic altered stress, a pathway contributing to preterm labor, but increase the risk of hypertensive disorders, metabolic syndromes and other complicating health factors.^{34,35,37} A fetus developing from a simple cellular organism to complex human within that environment, the prenatal status can contribute to organ developmental associated with hypertensive, metabolic, hypertensive and epigenetic changes, even among infants delivering at term. Preterm infants in general have high rates as adults of diabetes/ glucose intolerance and metabolic syndrome than predicted based upon family-genetic history. Breaking this cycle, make take more than one generation, and has a moral imperative above this critical health factor.

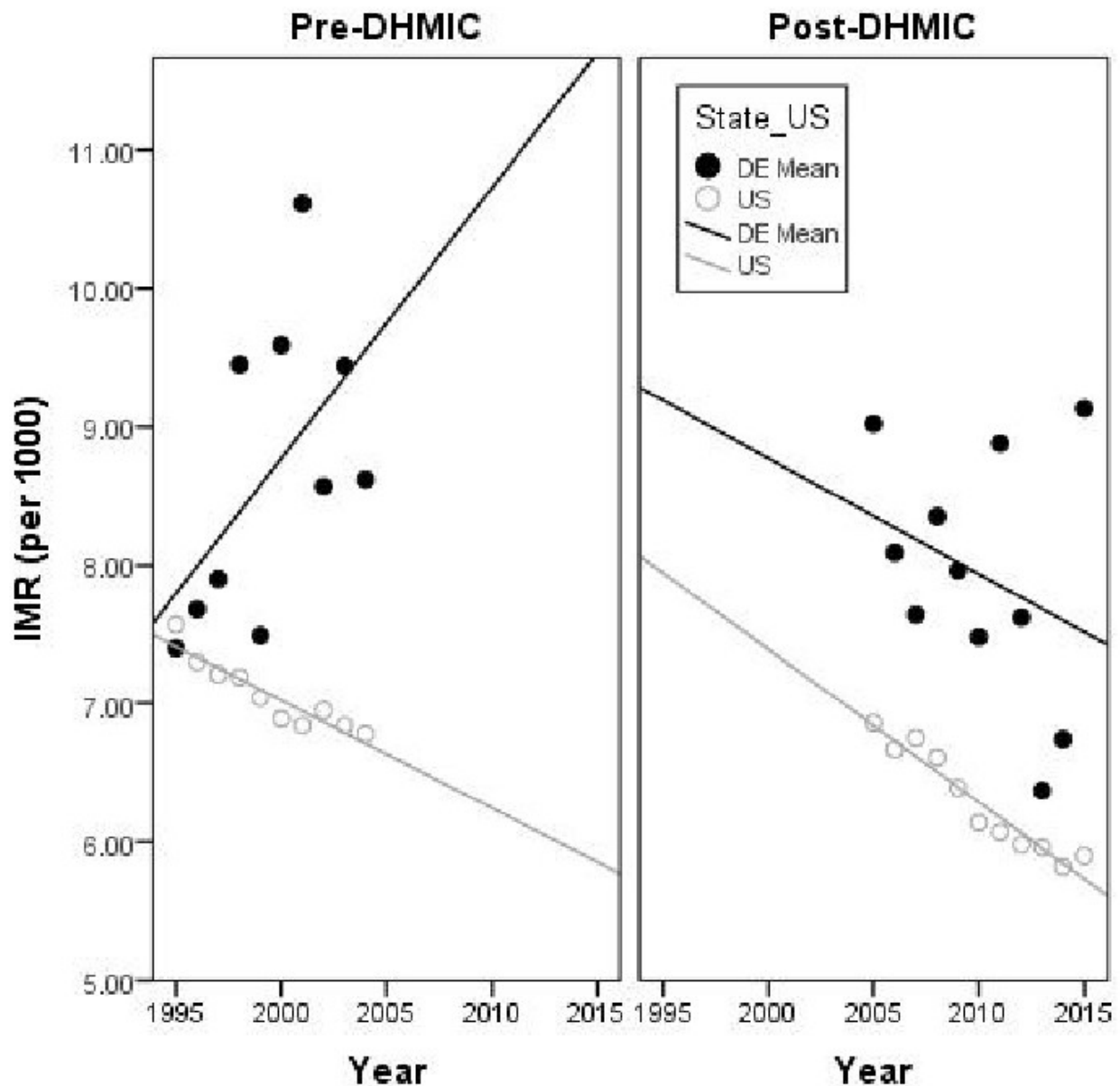
The health of all women prior to and during pregnancy is important. Among Whites and Hispanics, overweight and obesity are associated with adverse risks of pregnancy outcomes and higher rates of all cause NICU admission.^{6,7} Socioeconomic and underlying health factors and behavioral aspects (e.g. tobacco) are important and modifiable.^{12,31,40} In all groups, breastfeeding and human milk are important positive factors reducing the risk of mortality if premature, reducing the risk of SIDS in all gestational ages infants, and reducing the risk of serious infant infection.^{41,42}

A single early prenatal care visit may not alter the average healthy pregnancy. For other high-risk women, including women who do not realize their pregnancy is at high risk, comprehensive pregnancy, nutritional, emotional and global health support may be critical.^{5,20,21} The best medical evidence to date from combination of large epidemiologic studies, targeted interventions, and controlled mammalian models, indicate that optimally maximizing the health of mothers in the preconception period, ideally going back to when a mother was in- utero herself, can not only reduce IMR, but reduce the risks of premature birth and long-term health consequences in survivors and subsequent generations.³⁹

The precise reason for all cause higher rates of preterm birth in Delaware is not completely clear, but the DE Division of Public Health (DPH), Delaware Healthy Mother Infant Consortium (DHMIC), Christiana Care Health System (CCHS), Healthy Mothers Healthy Babies (HMHB),

and a multitude of non-profit stakeholders have engaged in activities to tackle the more modifiable underlying causes. Delaware's participation in Pregnancy Risk Association Monitoring System (PRAMS), a detailed CDC monitoring program, the Birth Defect Registry (BDR) and Fetal Infant Mortality Review (FIMR) permits a more detailed understanding of local process and influences that can help guide future interventions. These programs focusing on improved maternal and infant-childhood health may have a strong local impact. Prior to the creation of the DHMIC in 2005 by the Governor and Legislature, Delaware's IMR was rising while the US was experiencing a decline. Since 2005, with active investiture in the DHMIC and related programs, there has been a local Delaware reversal with a decreasing IMR trend (Figure 7).

Figure 7: DE IMR before and after the start of DHMIC in 2005



Two-thirds of DE's IMR occurs during the neonatal period (0-28 days of life). One-third of

infant mortality occurs later during the first year of life.² Delaware's postneonatal infant mortality rate has been declining in recent years and now similar to neighboring states (Figure 6). A portion of those infant's mortality is attributed to consequences of prematurity, congenital anomalies and aspects surrounding birth. Other high causes in Delaware are preventable conditions such sleep position-related and infections.² The childhood vaccine rate in Delaware is suboptimal, especially for conditions of early childhood including pertussis. Accidents and trauma during infancy remain leading and preventable causes of infant mortality at a national and local level. A highly modifiable factor to reduce late infant mortality (29-364 days) is adherence to the AAP infant sleep guidelines.^{43,44} The Delaware State Public Department, health providers, health entities and non-profit groups have helped advocate for safe sleep practices in accordance to AAP guidelines. In addition to safe sleep practice, other modifiable factors are important in reducing SIDS and sleep-related infant deaths. Tobacco increases the risk of SIDS four-fold.⁴³ Breastfeeding reduces the risk of SIDS by an equivalent amount.^{42,43} Breastfeeding also significantly reduces other infant mortality risks, especially infant infections. Breastfeeding supportive policies in the workplace that permit a mother to breastfeed or safely pump and store her milk are essential to maximize the health of infants and have been proven to be highly cost effective at an employer, employee and public health level.^{45,46}

Investiture in maternal-infant healthcare entities is crucial to achieve targeted low infant mortality rates, but this strategy cannot work in isolation.

Interventional strategies that globally address healthier communities including: a living wage, constructive paternal involvement and expanded healthcare access, especially to affordable preconception care, are essential to continually lower infant mortality rates. The average preterm infant costs \$66,742 (2017 dollars).⁴⁷ Extrapolating between 2007 and 2015, the cost of preterm infants in Delaware was \$869 million dollars. About half of premature infants are on Medicaid, yielding an estimated direct cost of \$435 million to the state. Doing nothing has direct costs to the state budget. In contrast, investing in these aspects has multiplier benefits beyond infant mortality. The emotional impact on families and communities is beyond calculation.

Delaware has an excellent healthcare structure, an involved and responsive state government, and activist community groups. Opportunities exist to meet and exceed targeted goals.

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