

# **Describing national trends in preterm infant mortality in the United States by race and socioeconomic status: a population study (1995-2020) of 100 million births**

## **Introduction**

Worldwide, prematurity is the leading cause of infant mortality<sup>1,2</sup>. Since the turn of the century, considerable advances in the field of neonatology have resulted in gains in preterm infant survival<sup>3-7</sup>. Despite its leading economic status, The United States (US) has one of the top ten preterm birth rates worldwide<sup>8-10</sup>, within which there are stark inequalities in the rates of preterm birth and mortality across socioeconomic strata, racial groups, and geographic regions<sup>11-15</sup>.

The objective of this study was to characterise trends in preterm infant mortality by maternal race and socioeconomic status, to assess how inequalities in preterm infant mortality rates have changed over a twenty-year period. US preterm-infant mortality rates have been reported on a yearly basis by the National Centre for Health and Statistics (NCHS)<sup>5</sup>, yet trends in preterm infant mortality have not previously been quantified by race and socioeconomic status at a national level over such a long period. This information is critical for providing public health officials, policy makers and clinicians with the information necessary to reduce health disparities, as well as determining the effectiveness of existing health policy.

## **Methods**

This is a retrospective longitudinal descriptive study of 100 million births across the US over a 26-year period using the US Period Linked Birth/Infant Death Dataset, compiled by the Centre for Disease Control and Prevention's (CDC) National Centre for Health Statistics (NCHS). The dataset contains linked infant birth and death certificates from all 50 US states and the District of Columbia. Between 1995 and 2020 two versions of the US standard birth certificate were used: the 1989 certificate and the 2003 revision, which introduced several new data items, and was implemented between 2003-2016. Within each infant's birth and death certificate, multiple variables, including maternal and infant characteristics, method of delivery, complications at birth, and underlying cause of death are available for analysis<sup>16</sup>.

Where the death occurs in a different state to that of the infant's birth, records are exchanged for linkage purposes, after which the NCHS performs follow-up linking for unlinked infant death certificates<sup>7,17,18</sup>. The data are then coded uniformly and rigorously quality controlled and, if required, the NCHS will impute missing data. These edited mortality and natality data files are used to create an annual national linked birth-death file for public use. Data from 1995 to 2020 were available at the time of completing this study.

### ***Defining Prematurity***

The World Health Organisation (WHO) definition of prematurity includes infants born alive before 37 completed weeks of gestation<sup>19</sup>. They further categorise preterm births, based on gestational age, into moderate to late preterm (32 to <37) weeks, very preterm (28 to <32 weeks) and extremely preterm (<28 weeks). The CDC national definition of “live birth” is determined by whether the infant shows signs of life at the point of delivery. This is not limited by duration of pregnancy and is subsequently adapted by individual US states as outlined in the CDC “State Definitions and Reporting Requirements”<sup>20-23</sup>. To mitigate the impact of non-viable gestations, we chose to only include babies born at  $\geq 22$  weeks. The definitions of categories of prematurity used for analysis are as follows:

- Total preterm (22 to <37 weeks)
- Extremely preterm (22 to <28 weeks)
- Very preterm (28 to <32 weeks)
- Moderately preterm (32 to <37 weeks)

### ***Subgroup definitions***

Subgroups were defined to ensure analogous information was present on both the 1989 and 2003 birth certificates. As maternal race and Hispanic origin are reported independently, race/ethnicity was split into ‘White Non-Hispanic’ (referred to as White), ‘Black Non-Hispanic’ (referred to as Black) and ‘Hispanic’. Factors related to maternal socioeconomic status used in analyses included maternal education, antenatal care, smoking and insurance status<sup>20-22</sup>. Two other important metrics of socioeconomic status, maternal income, and occupation were not available for analysis<sup>23,24</sup>. Smoking status was defined according to whether a mother had smoked one or more cigarettes at some point during the pregnancy. A mother’s education status was categorised according to the number of years of education completed, grouped into low (high school education or less), intermediate (high school graduate, associated degree, or some college credit) and high (completed a bachelor’s degree or higher). Antenatal care was categorised according to the Kessner criteria, determined by the number of antenatal care visits attended relative to the length of gestation<sup>25</sup>. Maternal insurance status was categorised as self-funded, private or government insurance (Medicaid and other government insurance types: Federal, State and Local), however was only available for analyses from 2011 onwards.

### ***Subgroup analyses***

The percentage of preterm births in each subgroup was calculated. Infant mortality was defined as death from 0 to 364 days after birth. Preterm infant mortality rates were calculated for each year between 1995 -2020, split into categories of prematurity, alongside each week between 22-27 weeks

to account for the large changes in mortality rate by week, at extreme gestations. To evaluate trends in preterm mortality rate, a Poisson regression model was used with year as a covariate to calculate a regression coefficient relating to the overall change in preterm infant mortality between 1995 to 2020. To counter year-to-year fluctuations, three-year average mortality rates for 1995-1997 and 2018-2020 were calculated with associated rate ratios, to evaluate the change in relative risk of mortality between subgroup categories and a chosen reference over time. All statistical and data analyses were performed using Stata 17.

## **Results**

### ***Maternal race and socioeconomic characteristics***

This study included 103,921,783 infants born across the USA between 1995 and 2020, of which 12,256,303 were born prematurely, and 437,650 preterm infants died within the first year of life. Baseline maternal characteristics changed over the study period. Maternal smoking decreased from 13.0% to 6.0%, the percentage of mothers with a Bachelor's degree increased from 22.1% to 33.5%, however antenatal care coverage remained broadly constant over time (table 1). Maternal racial composition changed, with a reduced percentage of White mothers (63.0% vs 59.5%), a comparable percentage of Black mothers (15.1% vs 16.0%) and an increased percentage of Hispanic mothers (16.8% vs 23.8%) (table 1).

### ***Premature birth rates***

Between 1995 and 2020, the percentage of premature births (22-37 weeks) gradually oscillated, with a peak of 12.7% in 2006. Consistent with reported patterns of preterm birth, we noted higher rates of preterm birth in mothers who smoked, were less educated, did not have private insurance and mothers who were Black<sup>26-28</sup>. Mothers receiving inadequate antenatal care consistently had the highest rate of preterm birth in any subgroup (table 1).

### ***Trends in preterm infant mortality***

During the study period, the total preterm infant mortality rate (IMR) decreased from 34.81 per 1000 preterm births (95% CI, 34.24 to 35.38) in 1995, to 22.35 (95% CI 21.89 to 22.80) in 2020. The greatest rate of improvement was seen in very and extremely preterm infants, among whom mortality rates increase steeply with decreasing gestational age. Very preterm IMR decreased from 53.08 per 1000 (95% CI, 50.92 to 55.25) to 36.12 (95% CI, 34.28 to 37.96), whilst extremely preterm IMR decreased from 352.60 per 1000 (95% CI, 343.79 to 361.40) to 246.61 (95% CI, 239.08 to 254.14). Separating each week of extreme gestation, the rate of improvement was notably less marked for those born at 22 weeks (regression coefficient -0.003 95% CI -0.004 to -0.002), compared to those born between 23 and 27 weeks (table 3). Although, moderately preterm IMR decreased relatively the

least (-0.008 95% CI -0.009 to -0.007), overall preterm IMR improved from 11.09 (95% CI, 10.74 to 11.44) to 8.00 (95% CI, 7.71 to 8.29).

### ***Trends in preterm infant mortality by maternal race***

Overall, Black infants were more likely to die following preterm birth than White and Hispanic infants across the study period, however once born extremely prematurely Black and Hispanic infants had a narrow survival advantage over White infants (table 2,3 figure 1). During the study, the total preterm IMR decreased from 31.59 per 1000 (95% CI 31.16 to 32.01) to 21.81 (95% CI 21.43 to 22.18) for White infants, 44.51 per 1000 (95% CI 43.74 to 45.27) to 31.09 (95% CI 30.44 to 31.74) for Black infants and 27.34 per 1000 (95% CI 26.62 to 28.06) to 20.13 (95% CI 19.63 to 20.62) for Hispanic infants. The rate of decrease in total preterm IMR was higher in Black infants (-0.015, 95%CI -0.016 to -0.015) than in White (-0.013, 95%CI -0.014 to -0.013) and Hispanic infants (-0.0010, 95%CI -0.011 to -0.009) infants; however, the relative risk of preterm IMR among Black and Hispanic infants compared with White infants remained the same (table 2). This trend was seen across all categories of prematurity (table 2), and therefore the proportional inequality in preterm infant mortality has remained constant over time. Once born extremely prematurely (22-27 weeks), the rate of improvement in preterm IMR was consistent between racial groups. There were also no changes in the relative risk of preterm infant mortality among Black and Hispanic infants compared to White infants (table 3).

### ***Trends in preterm infant mortality by factors related to maternal socioeconomic status***

Across all categories of prematurity, mothers receiving inadequate antenatal care had the highest preterm mortality rate (table 2), with mothers who smoked, who were less educated, or who lacked private insurance having higher preterm mortality rates within their respective categories. Again, once born extremely prematurely, mortality rates were comparable, except for infants who received adequate antenatal care, who had lower preterm IMRs than those who didn't (table 2, 3). During the study period, the rate of decrease in total preterm IMR was higher in non-smokers compared to smokers (-0.015 vs -0.010), higher in those with high levels of education compared to those without (-0.016 vs -0.010, -0.011), and higher in those who had received adequate antenatal care compared to those who did not (-0.014 vs -0.012, -0.013) (table 2). Correspondingly, the relative risk of total preterm IMR between these groups increased, amounting to a proportional increase in inequality over time (table 2). Across all categories, preterm IMRs decreased more greatly for very and extremely premature infants compared to moderately premature infants, except at very low gestational ages (table 2, 3). For those born extremely prematurely (22-27 weeks), the rates of improvement in preterm IMR were comparable between subgroups, and there were no differences in the relative risk of preterm infant mortality (table 3).

As analysis of Insurance status was only available from 2011 onwards; the trends in preterm IMR should be interpreted in this context. With respect to the total preterm infant mortality, the proportional inequality between mothers with private compared to government insurance remained constant, whilst inequality narrowed between mothers without insurance compared to those with government insurance (table 4). Again, once born extremely prematurely, preterm mortality rates were similar between different insurance groups, apart from at very low gestational ages (22, 23 weeks), where mothers with government insurance fared better. Over time, there were no differences between these groups in the trend coefficients or relative risk of infant mortality by week at extreme gestational ages.

## **Discussion**

This is the first population study to explore trends in preterm infant mortality in the US over two decades according to maternal race and factors associated with maternal socioeconomic status. Through the NCHS robust national birth statistics reporting, we have been able to include over 100 million births over a 26-year period. Our study shows that in the US, across all categories of prematurity, there has been significant improvement in preterm infant mortality. Yet, the rates of improvement have differed between population subgroups across gestational ages, with social and racial disparities in preterm health remaining present.

The improvement in preterm infant mortality rates in the US between 1995 and 2020 is a trend seen globally in high-income settings<sup>4</sup>. This reflects known improvements in multiple facets of obstetric and neonatal care during this period, including the use and timing of antenatal steroids, exogenous surfactant and other facets of respiratory care, alongside antibiotics, neonatal thermoregulation, and nutrition<sup>3,29-34</sup>. Other studies have demonstrated that these interventions have translated into reduced neonatal morbidity and improved neurodevelopmental outcomes<sup>29,35</sup>. These clinical and technological advances have been focussed on infants born at the extremes of gestation, where mortality rate is highest, reflected in the greater survival gains seen in very and extremely premature infants, most notably in those born between 23 and 27 weeks. The smaller survival gains seen in infants born at 22 weeks likely reflects the proximity to the limit of viability and the severity of the pathophysiology at such low gestations. Overall, the improvements in mortality at extreme gestational ages were most apparent from the early 2000s and appear to be continuing (figure 1). In contrast, despite overall reductions in preterm IMR for moderately premature infants, the rate of improvement appears to slow after 2005 (figure 1). This may suggest that we are close to reaching the natural limit in mortality reduction among the moderately premature infants, but considerable opportunity remains to reduce mortality rates among extremely premature infants. It will be instructive to see how this develops in subsequent years, particularly with increasing numbers of babies born at 22 weeks' gestation receiving active survival-focused care.

Understanding and reducing racial inequalities in preterm infant health is a major public health issue in the US. It is already known that Black infants are 1.5 to 2 times more likely to be born prematurely than White infants, with higher proportions of multiple births among Black infants<sup>5,6,36-39</sup>. The aetiology of these differences is believed to be multifactorial; however, the relative contribution of genetic, physiological, and sociological factors is debated<sup>26,36,40-43</sup>. Although studies of population based datasets have looked at racial disparities in preterm mortality and morbidity, this is the first study to quantify this over two decades at a national level in the US<sup>44,45</sup>.

Our trend analyses demonstrate that the absolute improvement in total preterm IMR was greater for Black infants than for White and Hispanic infants, however the proportional inequalities have remained constant over time with the overall risk of premature infant death in Black infants remaining approximately 1.4 times higher than for White infants. This difference has generally been attributed to a higher proportion of Black infants being born at the extremes of prematurity<sup>46</sup>. Indeed, our analyses show that once born very or extremely prematurely, Black, and Hispanic infants had a slight survival advantage compared to White infants. This may be due to differences in the aetiology resulting in extreme prematurity between different racial groups. Indeed, it has been suggested that the balance between maternal vs. infant ill-health as the cause of prematurity may vary between racial groups<sup>45</sup>. These trends in mortality rates for extremely premature infants have persisted over time, with similar survival gains seen between racial groups. Similarly, although Black infants born moderately prematurely had a higher risk of death, their survival gains were equivalent to White and Hispanic infants. This suggests that, at a national level, once born prematurely the neonatal care received by different racial groups is broadly equitable, despite regional, and neonatal centre-specific health disparities being previously reported<sup>51-53</sup>. Thus, it appears that all racial groups can access the advancements in neonatal care which account for the majority of improvement in preterm infant survival.

Regarding socioeconomic factors, our findings are consistent with previously reported disparities in both preterm birth rate and infant mortality, in relation to mothers' education, insurance, antenatal care and smoking status<sup>47-49</sup>. From the characteristics assessed, antenatal care status was the biggest predictor of both preterm birth and preterm infant mortality. Within our analyses, antenatal care status was the strongest marker of deprivation, with complex financial, structural and geographical barriers all contributing to mothers' ability to access adequate antenatal care<sup>50,51</sup>. The widening inequality in preterm mortality is unsurprising given that mothers unable to access antenatal care would not have benefitted from advances in antenatal care practice. This adds to an economic case for free antenatal care for all pregnant Americans<sup>52-54</sup>. Although we note increasing levels of maternal education, the widening inequality in preterm infant mortality amongst mothers with differing educational attainment confirms the relationship between education status and maternal and child health<sup>55</sup>. Regarding insurance status, equitable gains were seen amongst the different insurance groups, with the relative inequality remaining constant. Further expansion of government insurance provision to those without insurance remains important, although previous studies have debated the impact of the expansion of Medicaid on infant mortality<sup>56,57</sup>.

As seen with maternal race, once born extremely prematurely, preterm infant survival was comparable between subgroups, with equitable reductions in mortality rate over time. This again suggests that at a national level, most infants receive equitable neonatal care once born. However, further analysis of

the aetiology resulting in extreme prematurity between groups would aid interpretation of this finding<sup>31–33</sup>. Overall, this finding emphasises the importance of preventing infants being born at extremely early gestational ages as a means of reducing inequalities in preterm mortality rates between mothers of differing racial and socioeconomic groups. This highlights the need for targeted healthcare and economic policy focussed on preventing prematurity to reduce social and racial disparities in preterm health. The gestational age at which an infant is born remains the major determinant of their risk of death

### **Strengths and Limitations**

The key strengths of our study include the size and validity of the NCHS US Period Linked Birth/Infant Death Dataset, the length of time over which the study extends, and the variety of maternal characteristics assessed. Our study has several limitations. Firstly, we were unable to calculate adjusted odds ratios to account for confounders due to the separation of files containing the denominator (live births) and numerator (infant deaths) data. This meant our analyses were limited to reporting overall unadjusted trends, and could not explore the causation for changes in infant mortality rates. Secondly, despite the CDC national definition of “live birth” remaining consistent across the study period, we were unable to account for inconsistencies in the interpretation of “live birth” between US States<sup>58–60</sup>. We sought to mitigate this by using a 22-week gestational age cut-off, alongside reporting national trends. Lastly, further trend analyses according to maternal comorbidities such as diabetes, hypertension, and obesity would have been instructive. Uncontrolled maternal comorbidity negatively impacts preterm infant health and may represent an important route through which both a lack of antenatal care, alongside a mother’s socioeconomic status, result in an increased risk of preterm birth and mortality<sup>61–63</sup>. Better indices of SES, such as maternal occupation and income, alongside indexes of deprivation, such as the Multidimensional Deprivation Index (MDI), were not available in the dataset<sup>64</sup>. Additionally, we were unable to perform State-level analysis. This would have allowed assessment of regional inequalities which have been previously reported<sup>65,66</sup>.



### **Concluding remarks**

This population-level study analyses trends in preterm mortality within the US over the last quarter of a century. Overall, we highlight considerable progress: our results demonstrate a steady improvement in preterm mortality rate across all categories of prematurity. Yet racial and socioeconomic disparities persist. Our findings suggest that the proportional inequalities in total preterm IMR between Black and other racial groups have remained constant over time. Unfortunately, we found an overall widening of the inequality in preterm mortality in those from socioeconomically disadvantaged groups. Our results confirm the critical importance of mothers receiving antenatal care.

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