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STATE-OF-THE-ART

Infant mortality in the United States

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The infant mortality rate (IMR) of 6.0 per 1000 live births in the United States in 2013 is nearly the highest among developed countries. Moreover, the IMR among blacks is >twice that among whites—11.11 versus 5.06 deaths per 1000 live births.This higher IMR and racial disparity in IMR is due to a higher preterm birth rate (11.4% of live births in 2013) and higher IMR among term infants. The United States also ranks near the bottom for maternal mortality and life expectancy among the developed nations—despite ranking highest in the proportion of gross national product spent on health care. This suggests that factors other than health care contribute to the higher IMR and racial disparity in IMR. One factor is disadvantaged socioeconomic status. All of the actionable determinates that negatively impact health—personal behavior, social factors, heath-care access and quality and the environment—disproportionately affect the poor. Addressing disadvantaged socioeconomic status by improving access to quality health care and increasing social expenditures would have the greatest impact on the USA's IMR and racial disparity in IMR.

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INTRODUCTION

Of interest to policy makers is the high infant mortality rate (IMR) in the United States relative to other developed countries, despite spending the largest proportion of the gross national product on total health expenditures.[1] In this paper, we contrast the IMR in the United States with other countries, discuss the racial disparity in IMR in the United States and review causes of infant mortality to understand factors that may contribute to the higher IMR in the United States and racial disparity in IMR.

IMR IN THE UNITED STATES

Despite rising preterm birth (PTB) rates through 2006, the IMR in the United States declined from 1980 to 2013, from 12.6 to 6.0 per 1000 live births.[2] Nevertheless, in 2013 the IMR in the United States was the third highest among Organization for Economic Co-operation and Development (OECD) countries[3] (Figure 1). Of concern, also, is the racial disparity in infant mortality in the United States. In 2013, the IMR for infants born to non-Hispanic black women was more than double the rate that of infants born to non-Hispanic white mothers—11.11 versus 5.06 deaths per 1000 live births, respectively.[2] Infant mortality was also higher for infants born to American Indian or Alaskan Native mothers—7.61 deaths per 1000 live births. Infant mortality for infants born to Hispanic and Asian or Pacific Islander mothers—5.0 and 4.07 deaths per 1000 live births, respectively. In 2010 to 2013, the stillbirth rate was also higher among black and American Indian or Alaskan Native mothers (10.53 and 6.22 per 1000 live births plus stillbirths, respectively) compared with among white mothers (4.88 per 1000 live births plus stillbirths).[6]

FACTORS CONTRIBUTING TO THE USA'S HIGH IMR AND RACIAL DISPARITY IN IMR

The relation of high-PTB rate and high IMR

From 1981 through 2006, PTB rates in the United States steadily increased from 9.5% to 12.8%;[7] since 2006, PTB rates declined to 11.4% in 2013.[8] Despite this decline, the USA's PTB rate remains one of the highest in comparison with most other industrialized countries. In 2010, excluding births at <24 weeks (Live births <24 weeks were excluded because of likely differences in registration practices in registration of early births and deaths[4,5]), the USA's PTB rate was higher than those in 19 European countries.[9]

Because nearly 70% of infant deaths occur among infants born preterm,[10] the higher PTB rate compared with other industrialized countries is a significant contributor to the higher IMR in the United States. The higher IMR owing to PTB in the United States could be due to differences in gestational age (GA) distribution or the differences in GA-specific mortality. In general, the former is a function of maternal well-being, whereas the latter is a function of obstetrical/neonatal care.[11] Table 1 compares the GA-specific IMR in the United States in 2010 with those of 11 European countries.[9] The United States IMR was the fifth lowest of the 12 countries at 24 to 27 weeks and was the fifth lowest of eight countries at 28 to 31 weeks. At 32 to 36 weeks, the United States mortality rate was the second highest and was the highest at ⩾37 weeks (The relation of the prevalences of stillbirths and PTB at 32 to 36 weeks must be considered in interpreting these data. Lisonkova *et al.*[12] found an inverse relation between stillbirth and PTB rates at 32 to 36 weeks among 26 European countries and the United States, and speculated that obstetrical interventions were converting compromised fetus from stillbirths to PTBs). These data suggest that access to and quality of obstetrical and neonatal intensive care of preterm infants is not a major cause of the USA's excess

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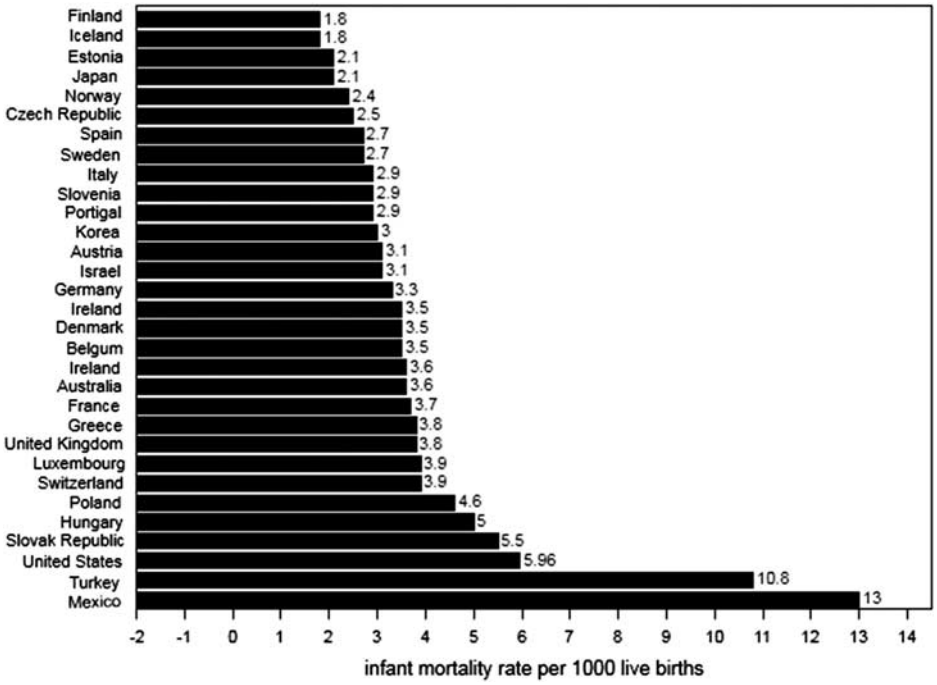

Figure 1. Infant mortality rates: selected Organization for Economic Co-operation and Development countries, 2013.[3] Live births < 24 weeks were excluded because of likely differences in practices in registration of early births and deaths.[4,5]

Table 1. Gestational age-specific infant mortality rates per 1000 live births in the United States and selected European countries in 2010 (ref. 9)

	Gestational age (weeks)			
	24–27	*28–32*	*32–36*	*⩾37*
Austria	217.39	34.38	8.01	1.24
Czech Republic	294.12	40.37	7.19	1.15
Denmark	198.80	[a]	7.95	1.11
England and Wales	245.17	48.29	8.73	1.60
Finland	203.25	[a]	9.74	0.97
Northern Ireland	325.00	[a]	[a]	1.96
Norway	189.78	[a]	9.87	1.06
Poland	428.32	98.98	15.43	1.95
Scotland	282.49	47.01	8.38	1.58
Sweden	165.08	35.14	8.33	1.10
Switzerland	308.41	41.75	6.77	1.12
United States	208.08	44.65	10.20	2.20

England and Wales provided 2005 data. [a]Figure does not meet the standards of reliability or precision; based on < 20 deaths in the numerator.

infant mortality. Rather a shift of the GA distribution of births toward more immature GAs compared with European countries is a more important factor. Therefore, understanding what variables may contribute to the higher PTB rate in the United States is relevant to any analysis of IMR rate in the United States.

Maternal smoking,[13] induced-PTB (both non-medically[7,14] and medically indicated[15,16]), induced ovulation and artificial reproductive technologies (ART),[17,18] multiple gestations unrelated to induced ovulation/ART,[19] teen pregnancy and advanced maternal age,[11] maternal obesity[20] and disadvantaged socioeconomic status (SES)[21] are the major factors associated with PTB. Chang *et al.*[22] estimated that non-medically indicated PTB, induced ovulation/ART, multiple gestations unrelated to induced ovulation/ART, medically indicated PTB, advanced maternal age and non-Hispanic black race together accounted for 50% of the increase in PTB rate from 1989 through 2004 in the United States.

Disadvantaged SES is associated with PTB, independent of race.[21] There is a high correlation between census tract poverty levels and PTB rates.[23] Although reduced access to care may contribute to this association, Foster *et al.*[24] postulated that this risk factor is largely socially-based, but biologically-mediated, maternal psychosocial stress (see Kramer *et al.*[25] for underlying biologic mechanisms). In a study from South Carolina,[26] women living in 'disadvantaged neighborhoods' were at increased risk for PTB. Maternal stress was also associated with PTB. However, stressful-life events were associated with higher risk of PTB only in mothers in the disadvantaged neighborhoods; no association was found between the risk of PTB and maternal stress in more advantaged neighborhoods. The authors suggested that these findings might be explained by lesser social and infrastructural resources to buffer stress, as well as harmful strategies for adapting to stress in disadvantaged neighborhoods. Indeed, in another study by the same group, the adjusted odds of having a PTB among mothers with low-social support were 1.9 times greater (95% CI 1.7, 2.1) than among mothers with high-social support.[27]

The relation of high-PTB rate to the racial disparity in IMR

In all, 55% of the racial disparity in IMR between blacks and whites is accounted for by preterm-related deaths.[28] The PTB rate was 13.2% among blacks compared with 8.9% among whites in 2014.[8] Moreover, the distribution of PTBs is shifted to more immature GAs and the disparity widens as GA decreases (Table 2). However, the racial disparity in IMR is not only due to a shift of the GA distribution to more immature GAs among blacks, but also to disparity in GA-specific mortality. In 2005 to 2009, the IMR was higher among blacks than whites for all GA categories and the

Table 2. Gestational age distribution of births by maternal race in the United States in 2014 (ref. 8)

Maternal race/ethnicity	*Gestational age (weeks)*					
	< 28	*28–31*	*32–33*	*34–36*	*37–41*	*> 41*
Non-Hispanic white	0.5%	0.7%	1.2%	6.5%	90.6%	0.5%
Non-Hispanic black	1.5%	1.5%	1.7%	8.4%	86.4%	0.3%
Hispanic	0.6%	0.8%	1.1%	6.5%	90.6%	0.3%

Table 3. Gestational age-specific infant mortality rates (per 1000 live births) by maternal race in the United States in 2005–2009 (ref. 29)

Maternal race/ethnicity	*Gestational age (weeks)*					
	< 32	*32–33*	*34–36*	*37–38*	*39–41*	*> 41*
Non-Hispanic white	90.1	19.3	7.8	2.9	1.7	2.7
Non-Hispanic black	105.0	20.5	10.2	4.3	2.9	3.9
Hispanic	92.3	20.0	7.7	2.4	1.5	2.9
Other race	121.4	24.1	10.1	4.3	2.2	3.7

disparity widens as GA decreases (Table 3).[29] These data suggest that access to and quality of health care also contribute to the racial disparity in the IMR.

Several factors contribute to this racial disparity in PTB. It is estimated that interpregnancy intervals < 12 months account for 8% of PTBs among black women compared with 4% among white women.[30] Fiscella[31] estimated that 50% of the difference in rate of PTB may be accounted for by the differences in urogenital infection rates. Although, the risk of PTB is greater for black women than white women at all ages, the risk of PTB increases at a greater rate with increasing maternal age in black women.[25] It is postulated that greater cumulative exposure of black women to risk factors throughout life is likely responsible for this increase.[32] Obesity contributes to the racial disparity in PTB because rates of obesity are highest among black women of childbearing age compared with white and Hispanic women.[33] Disadvantaged SES contributes to the increased-PTB rate among blacks.[26] This is likely in part due to decreased access to and lower quality of health care.[34–37] However, studies have shown persistent racial disparity in PTB in second-generation, high-income black women, even controlling for other known risk factors.[38–41] Collins *et al.*[41] compared PTB rates for black and white mothers, who resided in high-income neighborhoods in Chicago both at the time of their own birth and at the time of birth of their infant. Even after adjusting for maternal birth weight, age, education, marital status, smoking and prenatal-care utilization, the odds of second-generation high-income black mothers delivering a preterm, very low-birth weight infant were 2.4 times greater than those of second-generation high-income white mothers. These authors suggested that racial discrimination was a plausible explanation for this disparity. (See Dominguez[42] for a review of this construct.)

Studies have not supported race/ethnicity as a biologic/genetic risk, distinct from disadvantaged SES, for PTB. Race represents social, political and cultural stratification.[43] There is more genetic variation within than between races.[44] Epidemiologic data also refute the concept that genetics contribute significantly to racial disparity in PTB.[45] York *et al.*[46] reported that in addition to a higher PTB rate, the variance in GA among blacks is almost twice that among whites. They estimated that fetal genetic factors explained 3.7% of the variance in PTB rate among blacks and 35.2% among whites; maternal genetic factors explained 13.8% of the variation among blacks and 13.4% among whites. However, environmental factors explained 82.5% of the variance in PTB rate among blacks and 51.0% among whites. Any role for genetic risk factors is probably mediated by epigenetic changes or complete gene-by-gene or gene-by-environment interactions.[25]

The contribution of the higher IMR among full term infants to the USA's higher IMR and racial disparity in IMR

MacDorman *et al.*[9] estimated that, excluding births < 24 weeks gestation, 39% of the higher IMR in the United States compared with Sweden was due to the higher proportion of PTBs in the United States (9.8 versus 5.8%); however, 47% was due to the higher IMR for infants born at > 36 weeks gestation in the United States.

Nor does the increased prevalence of PTB and increased GA-specific infant mortality solely account for the racial disparity in IMR. The mortality rate due to all five leading causes of infant death was higher in blacks than whites in 2013.[6] Infant mortality per 100 000 live births in blacks compared with whites due to congenital malformations, deformations and chromosomal anomalies was 142 versus 115; due to disorders related to short gestation or low-birth weight was 261 versus 74; due to maternal complications of pregnancy was 86 versus 30; due to SIDS was 73 versus 40; and due to accidents was 63 versus 30.

The contribution of disadvantaged SES to the higher IMR and racial disparity in IMR

Among the 30 developed nations in the OECD, the United States ranks near the bottom not only for IMR, but also for maternal mortality and life expectancy from birth.[47] This suggests that endemic factors other than health care contribute to the higher IMR. One such factor is disadvantaged SES. All of the actionable determinates which negatively impact health—personal behavior, social factors, heath-care access and quality and the environment—disproportionately affect the poor.

It is likely that disadvantaged SES contributes to the higher IMR in the United States compared with other countries and to the racial disparity in IMR. In 2008, income inequality in the United States Gini coefficient (The Gini coefficient is a standard measure of income inequality which ranges from 0 (when everybody has identical incomes) to 1 (when all income goes to only one person).) was 0.38; of 21 other countries in the OECD for which data were available, only Mexico's and Turkey's coefficients were higher.[48] Yet, the percent of the gross national product expended on social service in the United States was 13.3, which was < 24 of the other 30 countries for which data were provided in 2005.[49] The USA's ratio of aggregate social service expenditures (Social service expenditures include public and private spending on old age pensions and support services for older adults, survivors benefits, disability and sickness cash benefits, family support, employment programs, unemployment benefits, housing support and other social policy areas excluding health expenditures) to aggregate health service expenditures (Health service expenditures include the public and private spending on curative care, rehabilitative care, long-term care, ancillary services, such as diagnostic imaging, laboratory test and patient transport; outpatient medical goods, prevention and public health services, health administration and health insurance and health care capital expenditures; and health care education and health care research and development) of 0.81 was the second lowest among 30 countries in the OECD. The ratio was lower only for Mexico at 0.78. The ratio was > 1.2 in the remaining 28 countries. In a regression model adjusted for gross national product per capita, higher social expenditures and a higher ratio of social to health services

expenditures was associated with lower IMR, but health service expenditures were not.[49]

STRATEGIES TO DECREASE THE IMR IN THE UNITED STATES

Shifting the distribution of PTBs to more mature GAs would reduce IMR in the United States. Unfortunately, the likelihood of this is limited by our poor understanding of the causes of PTB. Moreover, of the three interventions proven to be effective in decreasing the risk of PTB—reduction of antenatal smoking,[50] progesterone[51,52] and cervical cerclage[53]—the latter two are applicable to only a fraction of women at risk for PTB. Reduction of antenatal smoking, elimination of non-medically indicated PTB[54] and more responsible use of induction of ovulation/ART[55] will have a greater impact on PTB rates.

Because black infants have twice the IMR of whites, reduction in the racial disparity would also reduce the IMR in the United States. It is notable, however, that the IMR for infants born to white mothers in 2014 (5.06 per 1000 live births[2]) was still >27 other countries in the OECD (Figure 1).

Congenital anomalies were second to PTB as the leading causes of neonatal mortality, accounting for 21.7 and 47.3% of neonatal deaths, respectively, in the United States in 2009.[56] Sudden infant death syndrome (SIDS), congenital anomalies and unintentional injuries were the major causes of postnatal mortality, accounting for 22.2, 17.2 and 11.5% of postnatal deaths, respectively.[56] Therefore, strategies to reduce PTBs will have the greatest impact on neonatal mortality and the racial disparity in neonatal mortality, but will have little impact on postnatal mortality. Strategies to reduce deaths due to congenital anomalies and SIDS will impact neonatal mortality, postnatal mortality and the racial disparity in IMR. More attention is being focused on disadvantaged SES and racism as fundamental factors in the USA's high IMR and racial disparity in IMR. Addressing disadvantaged SES by increasing and improving access to quality health care and social expenditures in the United States would have the greatest impact on deaths during the neonatal and postnatal periods, and the racial disparity in IMR. Addressing racial discrimination (although a much greater challenge) might also reduce the IMR and the racial disparity in IMR independent of addressing disadvantaged SES.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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