Narrative Synthesis of Risk Factors for Infant Mortality

Among African American and Rural Populations in the U.S.

A report to Maryland Health Care Commission
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The following review has been completed for the Maryland Health Care Commission (MHCC), pursuant to legislation (2018 Md. Laws, Chap. 83), requiring the Commission to conduct a literature review to find appropriate national data on "factors, beyond the known factors of low birth weight, teen pregnancy, poor nutrition, and lack of prenatal care, affecting the mortality of African American infants and infants in rural areas in the United States and in the State" (2018 Md. Laws, Chap. 83, §1(b)(1)). This work will complement work being done by MHCC and Maryland Department of Health (MDOH) staff on state data related to infant mortality. This literature and the data analytics findings will be incorporated in the final report.

INTRODUCTION

In 2017, Maryland's infant mortality rate of 6.4 per 1,000 births ranked 33rd among US states. Since 2014, Maryland's infant mortality rate (IMR) has remained stable at about one percentage point above the national average. This IMR translated to 1,908 preventable deaths between 2014 and 2017. Despite recent reductions in infant mortality rates, Maryland remains somewhat short of the *Healthy People 2020* benchmark rate of 6.0 deaths per 1,000 live births. This burden of infant mortality is borne disproportionately by people of color. In particular, non-Hispanic Black infants have the highest risk of death during the first year of life. In the US, infant mortality rates for non-Hispanic Black infants have remained 2.3 times higher than the risk for non-Hispanic White infants. While this racial disparity in IMR is somewhat less pronounced in Maryland, the IMR among infants born to non-Hispanic Black Marylanders (10.5 per 1,000) remains over twice larger than IMR among infants born to non-Hispanic White women residing in the state. Moreover, this disparity in the risk of mortality between Black and White infants has increased recently as Black infants are yet to experience the declines in infant mortality rates that have been observed among White infants over the last decade. According to the MDOH, IMR among Black infants increased by 7% between 2016 and 2017. Moreover, while in Maryland (2013-2015) the burden of IM is somewhat higher in urban (6.7) than rural (6.1) counties,[1–3] in 2016, Black infants born in rural Maryland had an even higher IM (14.3) than Black infants born in urban counties (9.9).[4]

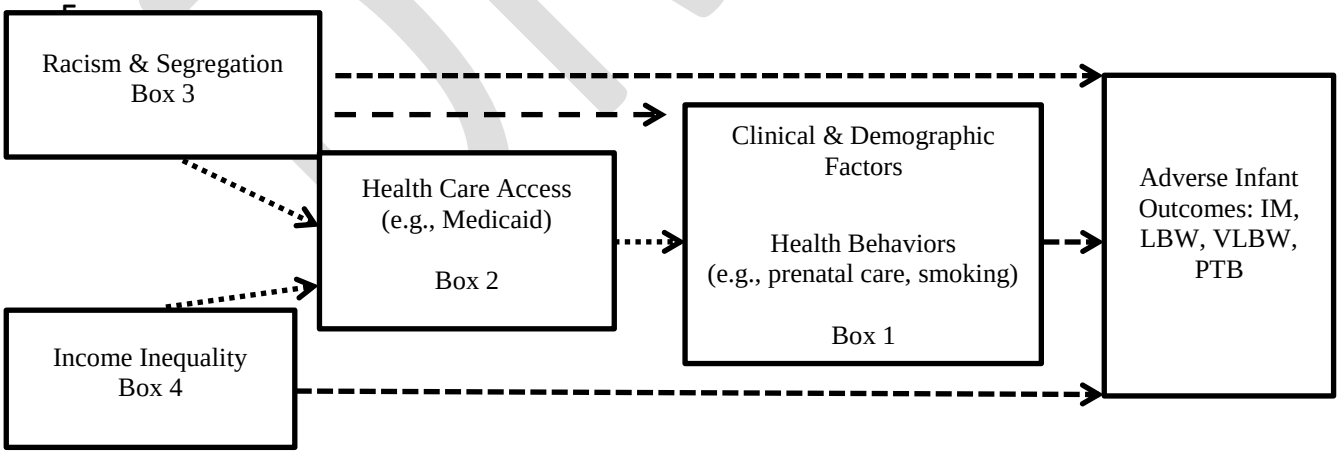
Estimates of percent reduction in IM by race and rurality among Maryland residents are also noteworthy. Between 2007-11 and 2012-16, in rural areas of Maryland, IM among Black and White residents decreased by <1% and 5% respectively. In contrast, in urban areas during that same time period, IM among Black and White residents decreased by 21% and 29% respectively. Overall, the high

risk of infant mortality, particularly among African Americans and in rural areas, remains a pressing public health concern in Maryland.

At the behest of the Maryland Health Care Commission, we have conducted a narrative review of the peer-reviewed literature (2008-2018) on risk factors affecting the mortality of African American and rural infants.

This review acknowledges the dynamic interrelations among various personal and environmental factors that drive determinants of infant mortality (Figure 1). In consultation with the leadership at MHCC, we have adopted a focus on individual-level clinical and demographic factors, health behaviors (Figure 1, Box 1), and access to health care (Figure 1, Box 2), all of which constitute measurable clinical and behavioral risks for outcomes related to and including infant mortality. Furthermore, we recognize that social determinants of health, particularly income inequality and structural racism, can have direct effects on the risk of infant mortality. However, our main focus is the effect of social determinants (Box 3 and 4) that are mediated through health care access. These determinants are important points of interception for implementing short-term reduction in IMR among the African American and rural populations in the face of limited resources. Finally, recognizing the similarities and overlap between risk factors of the known causes of infant mortality, we also considered determinants of some of these causes: preterm birth (PTB), pregnancy complications, sudden infant death syndrome (SIDS).[5]

Figure 1. Schematic of predictors of infant mortality



PRISMA review

In consultation with the University of Maryland's School of Public Health librarian, we developed a process for identifying and reviewing manuscripts that was informed by the

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[6] We searched PubMed and Embase for peer reviewed manuscripts that were published between January 1, 2008 and December 31, 2018, using combinations of Medical Subject Heading (MeSH) terms and subject headings to identify original research on risk factors for infant mortality. The following search terms were used in consultation with the authors of the complementary review on programmatic interventions to prevent infant mortality: "population, rural", "communities, rural", "African Americans", "black*", "risk", "risk factor", "characteristics, social", "determinant, mortality", "social determinants of health", "health disparit*", "social determinant*", "infant mortality", and "infant death." Manuscripts identified through this search were screened by title to exclude non-English, non-U.S. based, and duplicate studies. The remaining studies were included for abstract review in the secondary stage of screening.

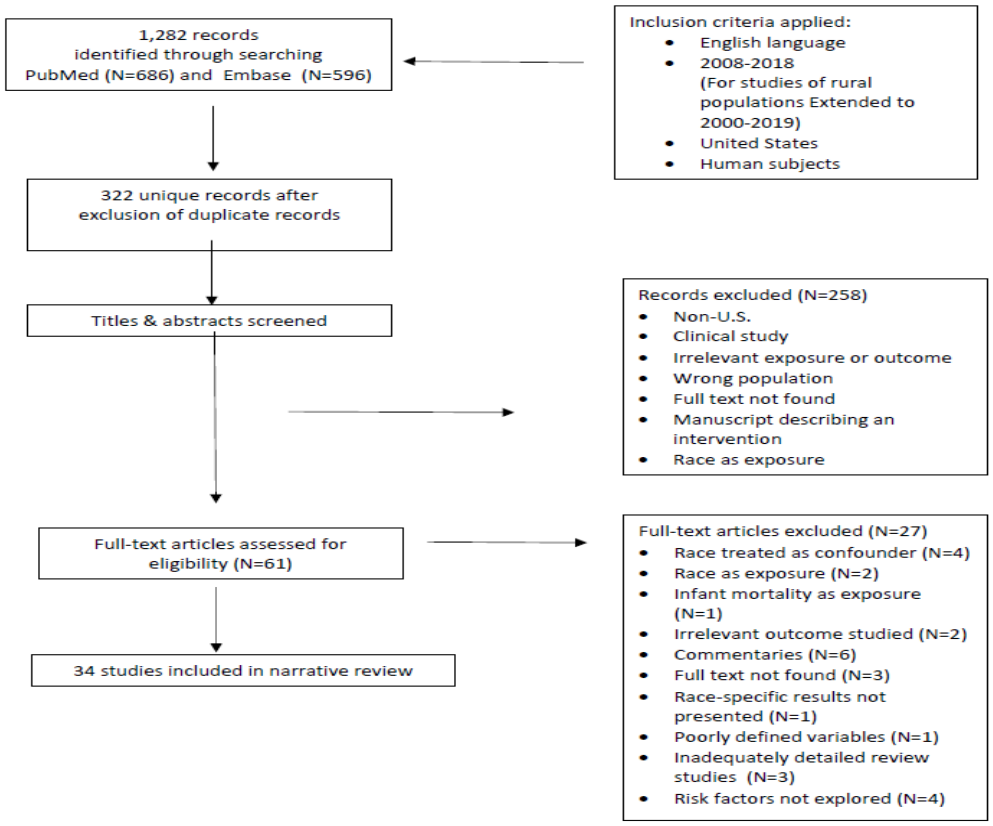
Abstracts were independently screened by two reviewers (De Silva; Nono), using Rayyan (rayyan.qcri.com), a web-based application specifically developed to facilitate systematic reviews. Manuscripts selected by both reviewers were advanced to full-text review, while studies with discordant results were resolved by consensus or by reviewing the full-text review together. Studies were excluded if either infant mortality or one of its known causes was not the outcome or were case studies. As we were specifically interested in the risk factors among African American and rural populations, we also excluded studies that considered race only as a covariate. Descriptive studies that only reported on infant mortality rates were also excluded.

Data extraction

Our search flagged 1,282 records cited on Pubmed and Embase, the majority of these records were cited in both databases (Figure 2). After removal of duplicate records, we identified 322 unique records for abstract review and screening of the title for non-US studies and removal of duplicate manuscripts. Weekly meetings were convened to review the extraction process and ensure agreement. During this process, 64 manuscripts were identified for full-text review and abstraction of information on study design, population, comparison groups, sample size, measurement of exposure(s) and outcome(s), and main effect estimates were extracted by one of three reviewers (De Silva; Nono; Takor). At this stage, an additional 27

manuscripts were deemed not to be relevant to the aims of this review and were excluded, resulting in a total of 34 manuscripts for inclusion. These studies were either specific to the African American populations or presented race-stratified results. We found only four studies of rural populations that met our inclusion criteria. For this reason, we expanded our search for studies of rural populations to peer reviewed and gray literature published between 2000 – 2019. The gray literature was limited to publications by federal or state governments or universities.

Figure 2. Schematic of studies included in the systematic review of risk factors of infant mortality.



Narrative Synthesis of Risk Factors for Infant Mortality

Among African American and Rural Populations in the US

Below we first provide a narrative review[7] of empirical studies among African Americans and then among rural populations. Studies of African American populations are ordered as follows (Figure 1): Individual-level clinical, demographic and behavioral factors, 2) access to health care and 3) social factors, specifically, racism, segregation and income inequality. These reviews are followed by a review of empirical studies conducted among rural populations. As detailed in the previous section, this review focuses on studies of infant mortality, preterm birth, low birth weight and very low birth weight.

A. Individual-level clinical, demographic and behavioral determinants

In line with an extensive body of literature dating back to the early twentieth century, studies reviewed in this section linked maternal demographic, health status, health behaviors and birth outcomes with the risk of infant mortality. Among these studies there was a focus on behavioral predictors of sudden infant death syndrome or suffocation while sleeping. This latter group of studies is presented separately.

Kitsantas (2008) examined disparities in neonatal (0-28 days) and post neonatal (28–364 days) mortality as well as predictors of causes of these two types of mortality among Black non-Hispanic and White non-Hispanic residents of North Carolina,[8] using data from the state's linked birth (N=813,733) and mortality (N=7,849) records (1999-2007). There was no excess risk of neonatal mortality among Black North Carolinians compared to the White residents (OR 1.03, 95% CI 0.96-1.11) independent of the known causes of IM (i.e., gestational age, birth weight, obstetric complications and inadequate prenatal care). In contrast, compared to Whites, Blacks experienced a 26% (95% CI 1.14-1.39) elevation in the risk of postneonatal mortality that was independent of these causes. Independent effects of these causes of IM and other individual-level risk factors are presented in Table 1. It is noteworthy that this study did not reveal a link between smoking during pregnancy and an elevated risk of neonatal mortality, but smoking predicted risk of postneonatal mortality. In this study, prevalence of smoking during pregnancy among the Black population was lower than among the White population (11% vs 16%).

Table 1. Causes, and other predictors, of mortality among Black neonates, post neonates and infants - North Carolina (1999-2007)[1]

	North Carolina (1999-2007)	
	Neonatal OR (95% CI)	Post neonatal OR (95% CI)
Age		
<18	0.94 (0.76-1.17)	0.81 (0.60-1.09)
18-26	Ref	Ref
27-34	0.98 (0.87-1.11)	0.68 (0.57-0.81)
>35	0.92(0.77-1.09)	0.68 (0.53-0.87)
Education		
< 9	1.06 (0.75-1.51)	**1.86 (1.26-2.77) 1.38**
9-11	0.99 (0.85-1.15)	**(1.14-1.68)**
12+	Ref	Ref
Unmarried	0.95 (0.73-1.25)	**1.26 (1.10-1.45)**
Parity		
0	Ref	Ref
1-3	0.85 (0.76-0.96)	**1.32 (1.11-1.56)**
>3	0.96 (0.85-1.10)	**1.84 (1.54-2.19)**
Prenatal Care		
Inadequate[2]	**1.35 (1.17-1.56)**	1.08 (0.88, 1.34)
Gestational age		
33-37 weeks	**1.38 (1.07-1.77)**	1.14(0.92-2.21)
<33 weeks	**3.65 (2.81-4.74)**	1.21 (0.88-1.64)
Live birth now dead	1.18 (0.96-1.46)	1.06 (0.75-1.48)
Birth Weight		
LBW	**5.63 (4.14-7.17)**	**2.95 (2.41, 3.61)**
Normal	Ref	
Obstet. Comp.	**5.63 (4.41-7.17)**	1.07 (0.94-1.23)
Diabetes	1.01 (0.76-1.35)	0.86 (0.55-1.33)
Anemia	0.98 (0.73-1.31)	0.92 (0.64-1.31)
Smoking		
Yes	0.88 (0.76-1.02) Ref	**1.65 (1.39-1.95)** Ref
No		

[1] Kitsantas & Gaffney (2008)

[2] Kessner's index

Another study of Black North Carolinians, conducted by Kitsantas & Gaffney (2010),[9] also used the linked birth infant data (1989-1997; N=811, 158) to investigate determinants of recognized causes of IM**:** conditions related to congenital anomalies (19%), short gestation/low birth weight (LBW) (49%), SIDS (14%), obstetric complications (9%) and infections (9.5%). Relative to White residents of North

Carolina, Black infants experienced a 20% excess risk of IM due to prematurity, 2.3% excess risk due to infections and 1.3% excess risk due to obstetric complications. In contrast, Black infants had a 6.3% lower risk for IM due to SIDS relative to White residents.

Of note is the strong association between having a history of a previous live birth ending in death and risk of IM in a second pregnancy. Among mortalities attributed to congenital anomalies, short gestation/LBW and obstetric complications, existence of a previous live birth ending in death (infants/child's age at the time of death was not reported) was the strongest risk factor (Table 2). The prominence of previous IM as a risk factor in this study of North Carolinians is noteworthy because in the previous study of North Carolinians by Kitsantas and Gaffney on which we reported (Table 1), prior IM did not appear as a risk of later IM. This may be due to the fact that Kitsantas and Gaffney considered overall (not cause specific) IM as the outcome of interest. Although less prominent, similar specificities are also apparent for the other risks assessed in this study. Considering this, specificity can be informative in targeting interventions of most prevalent causes of IM, which in this population was short gestation/LBW (49%). Below, we report on two other studies of the association between an early mortality (i.e., still birth and IM) with the risk of IM in a subsequent pregnancy.

Table 2. Associations of demographic and behavioral factors with known causes of IM –N. Carolina (1989-1997)[1,2]

	Infant Mortality Attributed to				
	Congenital anomalies	Short Gestation/LBW	SIDS	Obstetric Conditions	Infections
	OR (95% C)	OR (95% C)	OR (95% C)	OR (95% C)	OR (95% C)
Prenatal care[3]					
Inadequate	**1.23 (1.10–1.4)**	0.86 (0.76–1.03)	**1.49 (1.20–1.86)**	0.74 (0.54–1.05)	0.96 (0.73–1.27)
Adequate	Ref	Ref	Ref	Ref	Ref
Live births now dead					
At least one	**2.19 (1.43–3.35)**	**1.47 (1.30–1.67)**	0.89 (0.44–1.81)	**5.29 (3.37–8.32)**	1.16 (0.37–3.66)
None	Ref	Ref	Ref	Ref	Ref
Tobacco use					
Yes	1.06 (0.83–1.38)	**1.25 (1.07–1.47)**	**2.13 (1.67–2.71)**	1.35 (0.93–1.96)	**1.54 (1.12–2.13)**
No	Ref	Ref	Ref	Ref	Ref
Parity					
0	0.98 (0.80–1.22)	**1.47(1.30–1.67)**	0.58 (0.45–0.75	**2.05 (1.52–2.77)**	1.23 (0.90–1.67)
1-3	Ref	Ref	Ref	Ref	Ref

[1] Kitsantas & Gaffney (2010).

[2]Models include maternal age, education and use of Medicaid. [3] inadequate prenatal defined as care that started after first trimester or none, adequate defined as prenatal care started in the first trimester.

Two studies of infant mortality among Missourians utilized the State's linked birth and mortality data files (1989–2005). August et al. examined the association between stillbirth in a first pregnancy and risk of IM in a second pregnancy (n= 322,453) among infants with a gestational age range of 20–44 weeks.[10] Salihu et al. (2011) examined the association between IM in a first pregnancy and risk of an incident IM in a second pregnancy (n = 320, 350).[11] Among Black residents of Missouri, stillbirth in a first pregnancy predicted an approximately two-and-a-half fold increase in risk of IM in a second pregnancy (OR 2.68, 95% CI 1.41 –5.09) and a previous IM predicted over a four-fold (OR 4.28, 95% CI 2.61-6.99) elevated risk of IM in a second pregnancy. Both of these associations are independent of a number of individual-level determinants of IM (Table 3). The literature does not suggest biologically plausible pathways linking infant mortality in one pregnancy with risk of IM in a subsequent pregnancy. Consequently, and as noted above, prior stillbirth as a risk factor currently does not have a clear public health application other than consideration of a prior history of IM as a means of identifying high risk women. It is estimated that intrapartum stillbirths represent as many as one out of every three stillbirths worldwide; thus, highlighting the importance of appropriate care.

Table 3. Association between a prior IM and risk of stillbirth among Black and White[1] women – Missouri (1989–2005)

	Stillbirth HR[2] (95% CI)
Race	
Black	**2.06 (1.78–2.39)**
White	Ref
Maternal age	
<35 years	1.17 (0.98–1.39) Ref
≥35 years	
Education	
< HS	0.99 (0.85–1.17)
≥ HS	Ref
Marital status	
Unmarried	**1.34 (1.16–1.55)**
Married	Ref
Obstet. Comp.	
Yes	**3.48 (2.99-3.98)**
No	Ref
Prenatal Care	
Inadequate	**1.68 (1.50–1.89)**
Adequate	Ref
Pre-preg. BMI	
≥ 30 (obese)	1.05 (0.91–1.20)
<30	Ref
Prenatal Smoking	
Yes	**1.71 (1.501.95)**
No	Ref

[1]Salihu et al. (2011) - Race specific hazards for these covariates were not reported. August et al. did not report effect estimates for the covariates included in their hazard models.
[2]Hazard ratio

It is noteworthy that all of these risks operated among both Black and White populations. Among Black women, age <20 (vs. 20-34) protected against IM attributed to short gestation/LBW and IM attributed to obstetric conditions (OR 0.65, 95% CI 0.42–0.97). This is consistent with other evidence (outside the scope of this review) of an excess elevation in the risk of IM with maternal age in Black relative to White populations.[12] The results further suggest that age was the main determinant of excess risk in distribution of predictors of cause-specific IM among Black infants.

Zhang et al. (2011) examined risks of IM among residents of Mississippi utilizing the state's linked birth and infant death files (N = 328,393).[13] During the study period (1996–2003), Black infants were 70% (95% CI 1.5–1.9) more likely to perish than White infants independently of all sociodemographic, behavioral and medical risks. In addition to traditional risk factors, these authors also examined risk of IM associated with maternal diabetes (i.e., juvenile or adult onset diabetes; gestational diabetes, high blood sugar, insulin dependent or non-insulin dependent diabetes) as well as chronic and/or pregnancy-associated hypertension (Table 4).

Table 4. Causes, and other predictors, of mortality among Black neonates, post neonates and infants - Mississippi (1996-2003)[1,2]

	Mississippi (1996-2003)
	Infant OR (95% CI)
Age	
<18	**1.1 (1.1–1.2)**
18-26	1.0 (0.9–1.0)
27-34	Ref
>35	1.2 (1.2–1.3)
Education	
< 9	
9-11	1.1 (1.0 – 1.3)
12+	Ref
Unmarried	1.0 (0.9–1.2)
Prenatal Care	
Inadequate[2]	**1.7 (1.5-1.9)**
Gestational age	
33-37 weeks	**3.0 (2.4-3.8)**
Diabetes	1.3 (0.9–1.7)
Hypertension	**1.2 (1.0–1.4)**
Smoking	
Yes[3]	**1.65 (1.30-2.15)**
No	Ref

[1] Zhang et al. (2011) [2]Models include preterm birth and LBW; effects not reported in the manuscript. [2]No prenatal care vs. care beginning in the1st trimester. [3]Average of effects for 1-9 and 10+ cigarettes/day

Black diabetic women did not evince an elevated risk for preterm birth or having a low birth weight baby compared to White women. However, Black hypertensive women were 2.0 (95% CI 1.9 -2.1) and 3.0 (95% CI 2.8-3.1) times more likely to have preterm birth or a low birth weight baby respectively. Of note is the protective effect of early prenatal (vs. no) care among hypertensive (OR = 0.70, 95% CI 0.49–1.0) and diabetic women (OR 0.55, 95% CI 0.32–0.97). In this study we see evidence of a link between hypertension and an elevated risk of IM, we also see evidence that early prenatal care can protect against the risk of IM. Together these two strands of evidence emphasize the importance of ready availability of prenatal care for all women, and particularly among women with chronic conditions. Adequate prenatal care would allow health care providers to identify risk factors, diagnose medical conditions and assist women in controlling blood sugar and blood pressure levels.

Alio et al. (2011) examined the association between paternal involvement (defined as presence of paternal information on the birth certificate) and risk of neonatal and postneonatal mortality[14] as well as recognized causes of IM,[15] using linked birth records for the State of Florida (N = 1,397,801; 1998-2005). Infants born to Black mothers with absent fathers experienced the highest risk of infant mortality. The risk among Black

mothers with absent fathers was most pronounced for neonatal mortality (Table 5, part A). Alio et al. also examined the association between paternal involvement and causes of IM (but not IM) among teenage Floridians (N=193,512; 1998-2007) (Table 5, part B).[16] For both age groups, the prevalence of father involvement was 17% among Black and 71% among White residents of Florida.

Table 5. Risk of neonatal, postneonatal mortality and other poor birth outcomes associated with paternal involvement among Black Floridians. A) adults (1998-2005); B) teenagers (1998-2007)[1]

	Father Involved[2, 3]	Father Absent[2, 3]
	OR (CI)	OR (CI)
A- Births to adults ≥20 years of age		
Mortality:		
Neonatal	**2.17 (1.99–2.36)**	**8.06 (7.28–8.93)**
Postneonatal	**1.79 (1.60–1.99)**	**5.01 (4.40–5.70)**
LBW	**2.22 (2.18–2.27)**	**2.73 (2.65-2.82)**
VLBW	**3.02 (2.89–3.15)**	**4.85 (4.56–5.15)**
PTB	**1.56 (1.54–1.59)**	**2.03 (1.98-2.09)**
VPTB	**2.74 (2.63–2.85)**	**4.38 (4.14–4.64)**
SGA	**2.24 (2.20-2.28)**	**2.35 (2.29–2.42)**
B - Births to teenagers <20 years of age		
LBW	**1.99 (1.89-2.09)**	**2.29 (2.16-2.43)**
VLBW	**1.71 (1.51-1.94)**	**2.78 (2.43-3.18)**
PTB	**1.40 (1.33-1.46)**	**1.70 (1.60-1.80)**
VPTB	**1.71 (1.53-1.93)**	**2.67 (2.35-3.03)**
SGA	**2.36 (2.26-2.46)**	**2.41 (2.29-2.53)**

[1] Alio et al. (2011)
[2]Referent group = White mothers in the father-involved group
[3] Models included maternal age, parity, smoking, education, marital status, adequacy of prenatal care, anemia, cardiac disease, diabetes, preeclampsia, chronic hypertension, renal disease, eclampsia, placenta abruption, and placenta previa. Risk ratios for these factors were not reported.

Paternal involvement likely promotes health during pregnancy indirectly through its behavioral and emotional correlates. For example, Floridians who had the father listed on the birth certificate were more likely to receive timely prenatal care and less likely to experience obstetric complications (this evidence is from the overall sample, race-specific evidence was not reported). It is possible that fathers,

through provision of financial and emotional support, reduce stress and promote pursuit of health promoting behaviors. This beneficial effect is likely to extend through the postpartum period with benefits for both the mother and infant. In the following section on accidental suffocation, we review further evidence supporting the notion that paternal involvement can protect against risk of infant mortality. At the same time, we acknowledge that an indication of paternal involvement on the birth certificate is a weak proxy for information on the extent and quality of such involvement. We can only conclude that on *average* infants of women without paternal involvement have an elevated risk of mortality. As such, lack of paternal involvement may serve as a means for targeting women in need of further support during pregnancy.

B. Behavioral predictors of SIDS or suffocation while sleeping

SIDS and suffocation while sleeping was the focus of much of the literature on behavioral risk factors published in the last decade.

Table 6. Predictors of accidental suffocation and strangulation related mortality among Black infants – US (2000–2002)[1, 2]

	OR (95% CI)
Age	
<20	**2.12 (1.42, 3.16)**
20-24	1.31 (0.97,1.77)
25-29	Ref
≥30	0.74 (0.51, 1.06)
Education	
<HS	**2.98 (1.52, 5.84)**
HS	**2.26 (1.17, 4.37)**
13-15	**2.08 (1.05, 4.11)**
≥16	Ref
Parity	
1	Ref
2	**1.96 (1.42, 2.72)**
3	**2.72 (1.89, 3.94)**
≥4	**4.43 (3.03, 6.50)**
Gestational age (weeks)	
20–33	1.28 (0.85, 1.93)
34–36	1.10 (0.79, 1.52)
37–41	Ref
prenatal care	
1st trimester	**1.70 (1.08, 2.68)**
None	Ref
Smoking	
Yes	**2.63 (2.04, 3.39)**
No	Ref

[1] Carlberg and Shapiro- Mendoza (2012)
[2]Model included variables for mother's place of birth, infant sex and congenital anomalies. The associations for these variables did not reach statistical significance.

Carlberg and Shapiro- Mendoza (2012) identified maternal and infant characteristics associated with accidental suffocation and strangulation in bed among US infants, using US linked infant birth and death certificate cohort files (N= 11,719,232; 2000–2002).[17] Compared to White infants, Black infants were 77% (95% CI 1.53-2.05) more likely to suffer suffocation or strangulation in bed independently of a number of risk factors (Table 6) that operated similarly among both Black and White populations.

Several other authors have explored correlates of sleep position. Using data from birth certificates and the Florida Pregnancy Risk Assessment Monitoring System (N = 2,791; 2004-2005), Broussard et al. (2012) identified predictors of whether infants were put to sleep on their back and whether infants slept in a shared bed.[18] Compared to White Floridians, Black Floridians were more likely to use supine (on their back) position only infrequently (OR 2.44, 95% CI 1.89–3.16) and to share a bed with their infant (OR 3.03; 95% CI 2.30–4.00), independently of other risk factors (Table 8). Black (61%) and White (35%) mothers reported infrequent use of the supine sleep position. The reported prevalence of frequent sharing their bed with their infant(s) was 67% among Black and 38% among White mothers. We also note the particularly high risk (OR 7.50, 95% CI 4.16, 13.53) of bed sharing associated with reports of depression.

Table 7. Predictors of sleep behaviors among Black respondents to PRAMS survey - Florida (2004-2005)[1,2]

	Infrequent back sleeping	Frequent bed sharing[1]
	OR (95% CI)	OR (95% CI)
Father acknowledged on birth certificate		
Yes	ref	n.s.[2]
No	**2.13 (1.52, 2.97)**	
Prenatal care		
1st trimester	n.s.[2]	ref
Later or none		**3.78 (2.24, 6.39)**
Breastfeeding		
None	n.s.[2]	ref
≤ 4weeks		**4.02 (2.48, 6.52)**
>4 weeks		**5.84 (3.71, 9.19)**
Depression during/after pregnancy	n.s.[2]	
No		ref
Yes		**7.50 (4.16, 13.53)**

[1]Broussard et al. (2012). [2] Models included maternal age, education, marital status, parity, pregnancy intention, use of WIC during pregnancy and method of payment for delivery. The associations for these variables did not reach statistical significance. [3] Magnitude of insignificant estimates were not reported in the manuscript.

Analyses of PRAMS data from Wisconsin (2007-2010; N = 2,486)[19] and Georgia (2004 -2011; N= 6595)[20] revealed similar racial-ethnic disparities in bed-sharing among residents of these two states. Significantly more Black mothers (Wisconsin: 71%; Georgia: 82%) reported 'ever' bed-sharing compared with White mothers (Wisconsin: 53%; Georgia: 82% - p<0.001). Among African American Wisconsinites,[19] only maternal age (0.96 0.93–0.99) predicted a *lower* likelihood of bed-sharing for each additional year. Partner-associated stress was associated with 79% (95%CI 1.22–2.63) elevation in the likelihood of bed-sharing among African Americans. Maternal education of 13–15 years (OR 1.99, 95% CI 1.16–3.42) and 16+ years (OR 2.67, 95% CI 1.14–6.27) predicted higher likelihood of bed-sharing. Among African American Georgians,[20] having infants younger <4 months (OR = 2.4, 95% CI 1.6–3.7), being pregnant later than wanted (OR 2.2, 95% CI 1.4–3.5), using WIC (OR 1.6, 95% CI 1.11–2.3) and having 3+ (vs. 1-2) dependents (95% CI 0.4–0.9), predicted an elevated likelihood of bed-sharing.

Table 8. Interaction between bed-sharing and other known risks of SIDS – Case-control study of Black infants – Chicago (1993–1996)

	SIDS OR (95% CI)[1, 2,3]
Risk Factors	
Used pillow(s)	**4.1 (1.4–11.5)**
Slept on a soft surface	**8.8 (3.5–21.7)**
Prone sleep position	**4.1 (1.7–9.7)**
Maternal smoking	**6.0 (2.7–13.4)**
Breastfeeding	1.1 (0.3–3.4)
Protective Factors	
No pillow	**2.9 (1.5–5.3)**
Slept on a firm surface	**2.0 (1.1–4.0)**
Used only 0-1 cover	**2.8 (1.5–5.2)**
Supine sleep position	**4.9 (1.6–14.7)**
Pacifier use	**2.1 (1.1–3.9)**

[1] Fu et al. (2010)
[2] Reference group: Infants who did not bed-share and did not have the listed exposure.
[3] Models included maternal marital status, education, and adequacy of prenatal care according to Kessner index.

No clear patterns emerge from the two studies conducted among residents of Wisconsin and Georgia. Moreover, the elevated risk among the more educated women is puzzling. The association between education and bed sharing is usually confounded by breastfeeding, which is positively associated with both education and bed-sharing. However, in this population, *current* breastfeeding did not predict risk of bed-sharing (OR 1.45, 95% CI 0.92–2.30). It is not possible to determine whether this lack of an association stems from not knowing the length of breastfeeding as this information was not assessed. For example, among Floridians, longer duration of breastfeeding predicted higher risk (Table 7). These unilluminating findings can be attributed, in part, to the authors' analytic approach. The authors simply used a backward elimination approach to the regression analysis rather than a modeling approach informed by previous research or motivated by a specific hypothesis. Given these shortcomings, the following study of physical characteristics of sleep areas is arguably most useful for purposes of this review.

Fu et al. (2010) conducted a population based case-control study of SIDS among Black participants in the Chicago Infant Mortality Study (N=389).[21] All infants were residents of Chicago at time of SIDS as determined by the Cook County medical examiner (1993– 1996). These cases were matched to controls by maternal race/ethnicity, age at death/interview, and birth weight (Table 8). Overall, bed-sharing was associated with a two-fold increase (95% CI 1.2-3.4) in the risk of SIDS. Among infants who were bed-sharing, risk of SIDS was further elevated among infants who were placed on a pillow or slept on a soft surface. Moreover, risk of SIDS associated with bed-sharing remained elevated even when infants were not using pillows, slept on a firm sleep surface, used only 0-1 cover, and slept on their back (Table 6, section on protective factors).

The odds ratios reported in table 8 are based on a separate model that included maternal marital status, education, and adequacy of prenatal care as measured by the Kessner index. A multivariate model that included all of the independent variables that appear in Table 8 plus covariates revealed the following associations among bed-sharing infants: soft sleep surfaces (OR 2.9, 95% CI 1.4–

6.3), not using a pacifier (OR 2.7, 95% CI 1.1–7.0) and maternal smoking during pregnancy (OR 4.0, 95% CI 1.9–8.5). In conclusion, the small sample size for this case-control study is reflected in the imprecise effect estimates. On the other hand, the statistically significant associations despite the limited statistical power are remarkable.

Finally Salihu et al.,[8] in their study of Missourians (reviewed in the previous section), reported that among deaths attributed to SIDS, smoking (OR 2.13, 95% CI 1.67–2.71), having less than a high school education (OR 1.73, 95% CI 1.22–2.44) and inadequate prenatal care (OR 1.49, 95% CI 1.20–1.86) were the most prominent risks.

Together the evidence on risks for SIDS is consistent in identifying smoking as a prominent risk for SIDS. It is also noteworthy that these studies implicate breastfeeding as a risk for suffocation and SIDS. Anecdotal evidence suggests that the association between breastfeeding and SIDS is due to mothers' sleepiness, mothers falling sleep with their infants on a couch or in bed. Together, this evidence suggests a promising point of intervention is to further educate parents on safe sleep recommendations made by the American Academy of Pediatrics (Table 9).[22] Beyond these important recommendations, providing low-income mothers of all races with an appropriate sleep space (e.g., portable or full-sized crib) may also be critical.

Table 9. Recommendations of the American Academy of Pediatrics for a safe infant sleep environment

1) supine sleep position
2) no bed sharing, but the infant should be in a crib close-by
3) provide a firm, snug-fitting mattress
4) avoidance of waterbeds, sofas, and soft mattresses, and
5) avoid pillows, quilts, comforters, and other soft surfaces
6) prevent smoke exposure

Discussion

We must consider the literature reviewed in this section on individual-level demographic, medical and behavioral determinants of IM in the context of its shortcomings and strengths. All the studies reviewed in this section used state-level data collected by Federal agencies. Birth and death certificate data are not rigorously evaluated; the reliability and validity of these data vary considerably among US states.[23] Of the risks that we have focused on in this review, maternal demographic

information and birth weight is considered to be reported reasonably accurately. In contrast, prenatal care and maternal medical conditions are generally considered to be recorded less accurately.[24]

On the balance, the reviewed evidence further confirms findings from an extensive literature on the importance of preventing the recognized causes of IM (i.e., preterm birth, low birth weight, SIDS, obstetric complications and accidents). We also found evidence implicating hypertension as a clinical factor predicting IM (we did not find any evidence of diabetes predicting IM). Adequate prenatal care was also consistently linked with lower risk of IM. This link between hypertension and risk of IM coupled with consistent evidence of the protective effect of early prenatal care further emphasizes the importance of such care. Timely and consistent prenatal care allows health care providers to identify risk factors, diagnose medical conditions and assist women in managing their clinical conditions (e.g., control blood pressure levels). Programs that provide social support, such as centering programs, can also help alleviate some of the adverse effects of not having a partner or help further involve a partner (adequacy of prenatal care is discussed in more detail below).

We also note that postneonatal mortality is often reflective of factors that occur after birth. We found consistent evidence of the importance of preventing smoking among all women. Given the evidence linking postpartum smoking to SIDS, it is noteworthy that a significant proportion of smokers who quit during pregnancy relapse during the postpartum period (not reviewed here), again highlighting the importance of providing early care that extends beyond the immediate postpartum period.[25] Relatedly, it is critical to promote safe sleep methods during the postpartum period. We also found evidence of a strong link between depression and bed sharing.[18] One likely reason why depression was not examined more extensively is that most of the reviewed studies utilized linked birth and mortality data that do not assess depression. We note maternal depression because of its well-established association with several maternal and infant factors that can potentially elevate risk of IM;[26] we are not suggesting that maternal depression is directly linked with the risk of IM. Finally, the Black-White disparities in IM highlight the need for culturally sensitive social marketing messages, utilizing social networking strategies and the internet.

C- Health Care Access

Cox et al. (2011) examined racial disparities in the adequacy of prenatal care (PNC) and the link between PNC and infant mortality in Mississippi, using the state's linked birth and infant death files (1996 -2003; N = 292,776).[27] Across all categories of prenatal care (as defined by the Kotelchuck index, (table 10), Black Mississippians consistently fared worse than Whites in regards to the adequacy of prenatal care they received. Among these Black women, inadequacy of prenatal care was an independent determinant of IM in a dose-response manner (Table 11).

It is noteworthy that intensive prenatal care was a stronger predictor of IM than even inadequate prenatal care. Intensive prenatal care is often recognized as a proxy for existence of medical conditions that can complicate a pregnancy. Among this sample, existence of medical risk was associated with an elevated likelihood that a woman received intensive rather than adequate prenatal care. However, the strength of this association was stronger among White women ($p<.001$). This disparity is driven, in part, by the considerably larger proportion of Black women (16.4%) who received inadequate care regardless of medical risk compared to White women (5.9%) – (M-H v2 = 910.9; $P<0.01$). Likewise, Black women with medical conditions (26.4%) were twice as likely to receive less than adequate prenatal care compared to White women with medical conditions (13.1%). However, multivariate statistical tests were not conducted to evaluate the independence of this association. We also note that compared to odds of IM among Black women (Table 11), the odds of IM among White women who received either intensive care (OR 1.8, 95% CI 1.6–2.1) or no care (OR 2.9, 95% CI 1.4-6.0) was considerably lower. Because the odds ratios among these two populations of women were estimated in separate models, this comparison should not be viewed as a formal statistical test. These findings reemphasize the importance of ready availability of adequate prenatal care for all women, and in particular, women with existing chronic conditions. That Black women are generally more likely to present with chronic conditions makes provision of prenatal care a likely effective intervention for prevention of poor pregnancy outcomes, including IM.

Table 10. Prenatal care utilization by maternal race - Mississippi (1996–2003)[1,2]

	Intensive	Adequate	Intermediate	Inadequate	No care
Black	30.4%	40.6%	10.9%	16.4%	1.6%
White	33.4%	51.0%	9.3%	5.9%	0.3%

[1] Cox et al. (2011)

[2] PNC assessed with the Kotelchuck index

Table 11. Risk of mortality among Black infants – Mississippi (1996-2003) [1, 2, 3]

	OR (95% CI)
Prenatal care	
Intensive	**2.3 (2.0–2.6)**
Adequate	Ref
Intermediate	**1.4 (1.2–1.8)**
Inadequate	**1.5 (1.3–1.8)**
No care	**5.4 (4.2–7.0)**
Tobacco use	
10+ cigarettes/day	**1.8 (1.4–2.3)**
1-9	**1.5 (1.2–2.0)**
None	Ref
Marital status	
Not married	1.0 (0.9–1.2)
Married	Ref
Maternal med. Risks[4]	
Yes	**1.4 (1.3–1.6)**
No	Ref
Maternal education	
<HS	**1.4 (1.2–1.6)**
High school	**1.2 (1.1–1.4)**
College	Ref

[1] Cox et al. (2011)
[2] Model includes maternal age
[3]PNC assessed with the Kotelchuck index
[4] Medical risk factor indicates any of the following conditions: anemia, acute or chronic lung disease, cardiac disease, diabetes, eclampsia, genital herpes, hemoglobinopathy, hypertension, hydramnios/oligohydramnios, incompetent cervix, history of previous large infant or preterm or small-for gestational-age infant, renal disease, Rh sensitization, uterine bleeding or other specified conditions that complicated a pregnancy

Table 12. Hospital characteristics predicting mortality among VLBW infants – NYC (1996-2001)[1, 2]

Hospital characteristics	Infant Mortality OR (95% CI)
Teaching hospital	
Yes	0.88 (0.70–1.10)
No	Ref
Ownership[2]	
Private nonprofit	
Public	Ref
Religious, private,	1.03 (0.80–1.33)
nonprofit	0.80 (0.57–1.13)
% of Medicaid cases:	
<42%	0.86 (0.68–1.09)
≥42%	Ref
NICU level	
Level 1–2	Ref
Level 3–4	0.81 (0.58–1.12)
VLBW volume/6 years	
>200	**0.77 (0.60–1.00)**
≤200	Ref

[1]Howell et al. (2008)
[2]Model includes individual-level demographics and risk profile.
[3]Ownesrship categories were not defined in the text. They appear to overlap.

Howell et al. (2008) examined whether differences in the quality of hospitals at which Black and White infants are born contribute to Black/White disparities in neonatal mortality among very low birth weight (VLBW) neonates born in 45 New York City hospitals (1996-2001), using New York City vital statistics records on all live births and deaths of VLBW (500-1499 g) infants (N=11,781).[28] Hospitals were ranked according to the ratios of their observed to expected neonatal mortality rates given the maternal and infant demographics and risk profiles of deliveries at each hospital. Next, Black VLBW infants were randomly allocated to each hospital in proportions equal to their White VLBW counterparts, assuming that Black infants would experience the same mortality rate as their White counterpart at that hospital, adjusting for their risk profile. According to the data, if Black women delivered in the same hospitals as White women, there would have been 6.7 fewer deaths per 1,000 births among VLBW Black infants. In other words, 35% of

the Black/White disparity in VLBW mortality rates in New York City is attributable to the differences in the hospitals where Black and White infants are born.

Of hospital characteristics assessed in this study, volume of VLBW deliveries was the only characteristic that was protective of mortality (Table 12). Black VLBW births were less prevalent (77%) at high-volume hospitals compared with White VLBW births (86%). If the Black and White VLBW infants were equally likely to be born at high-volume hospitals, then mortality rate for Black VLBW infants would decrease by 1.4%, reducing the Black/White disparity in mortality among VLBW infants by 10%.

Hutcheon et al. (2015) examined whether Medicaid funding for pregnancy termination of anomalous fetuses contributes to the Black–White disparity in IM due to congenital anomalies, using U.S. vital statistics data on deaths resulting from anomalies (1983–2004) and data from the Nationwide Inpatient Sample (2003–2007).[29] In 1983, women residing in states without Medicaid funding were 3% (95% CI, 1.01–1.05) more likely to have an anomaly-related IM than residents of states with such coverage; by 2004, this gap had grown to 21% (95% CI 1.18–1.24). This temporal change occurred among both Black and White infants, but Black women (65.8%) were more likely than White women (59.6%) to deliver in a state lacking Medicaid funding for pregnancy termination of anomalous fetuses ($p<.01$). The association between Medicaid funding for pregnancy termination of anomalous fetuses and risk of IM is race specific. Black infants born in states lacking Medicaid benefit were 94% (95% CI 1.52–2.36) more likely to die from an anomaly than Black infants born in states with such benefits. In contrast, among White infants, this relative risk was 49% (95% CI 1.32–1.65). In states with Medicaid funding, Black women not on Medicaid had a higher risk of IM than Black women on Medicaid (204.9 vs. 129.3/100,000).

Table 13. Existence of state office of minority health and Black IM and B/W IM ratio – US (1980– 2007)[1,2,3]

	Black IM	B/W IM Ratio
	ß	ß
State Office of Minority Health	**–0.75***	**–0.13***
State Office of Minority Health, years in existence	–0.04	–0.01
State minimum wage	-0.36*	-0.03
Medicaid spending	**– 3.30***	**–0.60***
Black poverty	0.03	0.01
Unemployment	**–0.30***	–0.01

[1] Patton et al. (2014)

[2]* $p<.05$

[3] Model also includes variables indicating state's political climate (conservative to liberal); per capita income; proportion of Black legislators; level of education of among White women and White poverty.

Patton et al. (2014) examined whether states with an Office of Minority Health (OMH) have lower Black IMRs (1980-2007) than states lacking such an office.[30] Patton et al found a contemporaneous protective effect for existence of an OMH office but not an effect associated with the years of existence of such an office. Of all the state-level

variables examined in this study, Medicaid spending had the most robust association with Black IM (Table 13). The study also found that when Medicaid spending is low, the implementation of a state OMH predicts decreased Black infant mortality; conversely, this effect diminishes with increasing Medicaid expenditure.

Conclusions from this study must be considered in the context of its shortcomings. Despite the careful inclusion of a large number of covariates in these analyses, several aspects of the study cast some doubt on its findings. The number of states included in the study and their demographic information are not presented in the study. Secondly, the observation that existence of state OMH offices influence Black IMR but not the IMR trend over time is not intuitive and the authors do not explain this discrepancy. Despite these shortcomings, it would be reasonable to suggest that these data highlight the relevance of Medicaid benefits as a means for reducing Black IMR.

Discussion

A consistent conclusion from the reviewed evidence is that access to quality health care can lower IM rates among Black infants. In this regard, access to prenatal care, especially for women with preexisting conditions, as well as access to quality hospitals is critical. A majority of women of all races receive postnatal care and have a doctor's visit in the first week after birth. These visits are opportunities to provide educational interventions on multiple levels, including information on avoidance of individual-level risks that we reviewed above as well as resources and information to promote health of the mother and infant during the first year postpartum.[25] This conclusion, however, is not particularly remarkable. What is important to reemphasize is that the protective effect of prenatal care on IM is more pronounced among Black infants than it is among White infants. This is because Black women are more likely to receive inadequate prenatal care regardless of medical risk. On the other hand, ready avenues exist for remediation of this disparity.

A majority of Black mothers use Medicaid to pay for delivery, making the Medicaid program a potentially viable route of administration of preventive and health promoting programs. However, this approach is limited in that it neglects women who do not receive postnatal care and most likely do not receive adequate or timely prenatal care either. Medicaid covers pregnancy services from diagnosis through only the sixth week post-partum. Women lacking prenatal care or coverage during the inter-conception period are among the highest risk groups for experiencing infant mortality. It is estimated that Medicaid programs can reduce healthcare costs by several millions of dollars by shifting to *preventive* strategies.[31] A change of focus on enhanced and early prenatal care to prevent risk factors for

IM and to promote health of the entire family during the first year post-partum is an approach that is supported by empirical evidence and has gained much currency in the last decade.[32] Retooling state's resources to focus on preventive and health promoting initiatives would be a fruitful area of collaboration between Maryland's Medicaid and the Office of Minority Health.

D. Social Determinants: Racism and segregation

Individual-level demographic and behavioral risks do not fully explain the persistent disparities in Black and White infant mortality rates in the US. Exposure to interpersonal racism and structural racism has been proposed as a biologically plausible determinant to explain health disparities and, by extension, the elevated risk of infant mortality that persists among Black Americans.

Lemon et al. (2016) estimated the excess risk in infant mortality attributed to race independently of pre-pregnancy obesity, using the linked Pennsylvania birth-infant death certificates (2003-2011; N=51,055,359 births) and fetal death certificates (2006-2011; N=53,102 stillbirths).[33] Pre-pregnancy BMI was classified as obese (BMI ≥30.0 kg/m2) or not obese (BMI<30 kg/m2) and severely obese (BMI ≥35.0 kg/m2) or not severely obese (BMI <35 kg/m2). The authors first estimated the excess risk of IM per 1,000 births associated with race via a model that included only race. The two subsequent models included terms for BMI (BMI≥30 and BMI≥35) and its interaction with race. The coefficient for race was interpreted as the race-related excess IM that was independent of pre-pregnancy BMI. No other covariates were included in the models because the authors argued that their interest was in race as a 'marker of disparity.'

In Pennsylvania, compared to White women, Black women experienced an overall excess 5.8 (95% CI 5.3-6.3) IM per 1,000 live births. After accounting for the risk attributable to pre-pregnancy BMI ≥ 30 and attributable to pre-pregnancy BMI ≥ 35, the excess risk of IM among Black infants changed to 5.2 (95% CI 4.7-5.7) and 5.5 (95% CI 5.0-5.9) infants per 1,000 live births respectively (Table 15). Similar estimates were made for neonatal and post neonatal mortality (Table 14).

These estimates and their interpretation are questionable. Interpretation of the variable race as a marker of disparity without controlling for other socio-demographic variables such as age, income, education, etc. renders a marker of disparity that is confounded by these other risks rather than allowing a measure of disparity that could reflect the lived experience of African Americans independently of these demographic markers of health.

Table 14. Excess risk of infant, neonatal and postneonatal mortality among Black infants relative to White infants - Pennsylvania (2003-2011)[1]

	Bivariate[2] Models	Excess risk[3] not attributed to pre-pregnancy BMI≥30	Excess risk[2] not attributed to pre-pregnancy BMI≥35
	Risk Diff. (95% CI)	Risk Diff. (95% CI)	Risk Diff. (95% CI)
Infant Death	5.8 (5.3-6.3)	5.2 (4.7-5.7)	5.5 (5.0-5.9)
Neonatal death	3.7 (3.3-4.1)	3.3 (2.9-3.8)	3.5 (3.1-3.9)
Postneonatal death	2.1 (1.8-2.4)	1.9 (1.6-2.2)	2.0 (1.7-2.2)

[1] Lemon et al. (2016) [2]Model includes only race. [3]Model includes BMI

Structural racism

1. Segregation

A key consequence of structural racism in the U.S. is diminished social and residential mobility that segregate Black Americans in relatively high poverty areas irrespective of their family income. For example, in the U.S., high-income White families reside in lower poverty areas than Black Americans with similar family income.[34] Black households earning >$75,000 annually reside in areas with about 15% prevalence of poverty, whereas, White households earning <$40,000 annually reside in areas with about 13% prevalence of poverty.[35] Consequently, within areas that appear to have the same degree of income inequality, Black families reside in relatively segregated areas with limited structural resources (e.g., safe public spaces ad quality educational opportunities).

There is strong evidence that residence in segregated areas limits access to health promoting resources and exposes individuals to stressful circumstances, even for middle-class residents of segregated areas who reside in proximity to poverty.[36] As such, the challenge in establishing a direct association between residence in segregated areas and risk of IM is disentangling any direct effect of segregation from its mediated effects through more proximal indicators of structural racism. Other concerns include the confounding effect of concurrent exposure to segregation and ecologic-level poverty, as well as proper accounting for individual-level risks. Below we review the recent studies (2008-2018) on the association between segregation, other indices of structural racism and risk of infant mortality (or its known causes). These studies have approached the challenges of assessing the association between structural racism and IM through different approaches, as discussed below.

Kramer and Hogue (2008) examined the association between two measures of segregation (i.e., evenness and isolation) and risk of a very preterm birth, using U.S. Linked Birth and Infant Death Data (2002–2004) across 168 metropolitan statistical areas (MSAs) with adequate numbers of Black residents to allow stable estimates.[37] Among this sample, residents of MSAs with the highest proportions of Black residents (39.2) and Black women living below the poverty line (37.5) had the highest risk of very preterm birth (vPTB). MSA's isolation levels, generally considered a measure of lack of access to population-level health promoting resources, was positively associated with Black vPTB rates (ß= 2.7, p<0.05). In contrast, cities' level of evenness, defined as the degree to which a minority group is evenly distributed across sub-areas of the MSA, was negatively (ß= -2.0, p<.01) associated with Black vPTB rates. These associations were independent of metropolitan population, census region, prevalence of college educated adults and median household income.

Two other findings from this study are also remarkable. First, the rate of vPTB in the very best MSA for Black women was the same as the rate in the very worst MSA for White women. Second, distribution of vPTB rates among MSAs was 2.5 times (p<0.001) greater among Black than White women, with the standard deviation for Black women approximately 2.5 times greater than for White women. This suggests that risk of vPTB among Black women is more sensitive to structural conditions of their area of residence compared with White women.

Table 15. Association between residence racially segregated and Black IM - US cities with a Population >250,000 (2000–2002)[1]

	Rate Difference[2] (95% CI)
Infant mortality	1.12 (-0.51, 2.74)
Postneonatal mortality	0.99 (-0.20, 2.17)

[1] Kramer and Hogue (2008)

[2]Rate difference between in IM per 1,000 between most and least segregated US cities. Model includes: Maternal age, education, marital status; parity, adequacy of prenatal care; father's age; low birth weight status; preterm birth status, and year of delivery.

Hearst et al. (2008) examined the association between segregation (i.e., isolation index) and IM among Black infants, using U.S. Linked Birth and Death records (2000–2002; N= 677,777) for Black infants residing in 64 cities with a population of at least 250,000 residents.[38] There were 1.12 excess infant deaths per 1,000 live births linked to residence in segregated areas. However, after adjusting for covariates (Table 15), no statistical difference in the number of infant deaths per 1,000 live births was found for Black infants born in segregated cities compared with those born in non-segregated cities. A separate analysis of postneonatal deaths due to SIDS, accidents, and assault also yielded null results. We note that the above two ecologic studies by Hearst et al. and Kramer et al., did not control for individual-level variables. The next study addresses this shortcoming with a hierarchical analysis.

Shaw et al. (2010) examined whether county-level prevalence of residents with the same ethnic background predicted risk of preterm delivery, low birth weight and IM among Black mothers and their infants, using U.S. Linked Birth and Infant Death Data (2000).[39] Among Black mothers (N= 581,151), ethnic density predicted risk of preterm birth and low birth weight but not IM.

Table 16. The association between ethnic density and birth outcomes among Black Mothers - US (2000)[1]

Ethnic Density:	Mortality OR (95% CI)	Preterm Birth OR (95% CI)	Low birthweight OR (95% CI)
0–0.99%	Ref	Ref	Ref
1–4.99%	1.03 (0.67, 1.57)	**1.26 (1.09, 1.44)**	**1.25 (1.08, 1.46)**
5–14.99%	1.14 (0.76, 1.72)	**1.31 (1.15, 1.49)**	**1.34 (1.16, 1.55)**
15–49.99%	1.18 (0.79, 1.78)	**1.38 (1.21, 1.58)**	**1.38 (1.19, 1.59)**
≥50%	1.18 (0.77, 1.79)	**1.37 (1.19, 1.57**	**1.35 (1.16, 1.57)**

Models include parity, maternal age, marital status, maternal education, maternal nativity, smoking status and County-Level Median Income

As described in Table 16, these associations were not linear. Black residents of counties with the lowest density of Black residents (0%–0.99%) had the lowest odds of LBW. A relatively small increase in the density of Black residents (1%–4.99%) corresponded with the largest increase in the risk for preterm birth and low birth weight; beyond this, increases in Black population density had little additional impact. The strength of this study was its hierarchical analysis that nested individuals within counties and included individual-level covariates, but this study did not control for individual-level correlates of income.

Mehra et al. conducted a meta-analysis of 42 studies, published prior to 2008, that examined associations between segregation and adverse birth outcomes among Black and White mothers.[40] Among Black mothers, residence in the most segregated areas compared to the least segregated areas predicted a modest elevation in the risk for preterm birth (OR 1.17, 95% CI 1.10, 1.26) and low birth weight (OR 1.13, 95% CI 1.06, 1.21). This evidence was consistent regardless of whether segregation was measured by clustering, evenness, concentration, centralization or racial composition. It is noteworthy that not all studies evinced a positive association between segregation and adverse birth outcomes among Black women. Of the 21 studies that conducted race-specific analyses, 13 studies found a null association between segregation and adverse birth outcomes among Black (or White) mothers. Eight studies reported an elevated risk among Black (and White) mothers, but these studies were judged to have been of poor-quality conducted at the ecologic level without controlling for individual-level factors. A common pattern among studies with discordant results by race was a finding of elevated risk of adverse birth outcomes among Black infants, and decreased risk or no risk among White infants.

2. Other measures of structural racism

Wallace et al. (2017) examined associations between overall and race-specific contextual measures of structural racism with the risk of IM among Black infants across the 50 U.S. states and the District of Columbia, using the U.S. linked birth/infant death files (N=95,554; 2010-2013).[41] The state-level indicators of structural racism were chosen because they reflect policies that dictate distribution of health promoting resources and opportunities (Table 17, part A). Race-specific Structural racism was operationalized as the ratio of Black to White population values for each of these indicators (Table 17, part B).

Among the Black population included in this study, there were no associations between overall state-level contextual indices and Black IMR, but there were modest associations between race-specific measures of structural racism and Black IMR (Table 17, part B). Consistency of findings across multiple measures of race-specific structural racism covering the entire continental U.S., along with inclusion of variables in the regression models to control for state-level poverty, make for a persuasive argument in support of the link between structural racism and risk of Black IM. However, the study's conclusions remain subject to caveats due to its ecologic design.

Table 17. Association between overall and race-specific state-level measures of structural racism and Black IMR– Fifty US states and DC (2010–2013)[1,2]

	Black Infant Mortality RR (95% CI)
A- Overall Measures of Structural Racism	
Prison incarceration	1.06 (0.96,1.16)
Juvenile custody	1.00 (1.00,1.00)
Unemployment	0.99 (0.88, 1.12)
Managerial employment	0.97 (0.91, 1.05)
Educational attainment	0.91 (0.80, 1.05)
Median household income	**0.83 (0.72, 0.95)**
B - Race-specific Measures of Structural-Racism	
%Black prison incarceration	1.02 (0.96,1.08)
%Black juvenile custody	1.00 (0.89,1.13)
%Black unemployment	**1.06 (1.00,1.12)**
%Black managerial employment	**0.91 (0.85, 0.99)**
%Black educational attainment	**0.85 (0.78, 0.93)**
%Black median household income	**0.86 (0.77, 0.98)**

[1] Wallace et al. (2017)

[2]Models included % of state population living in poverty

In another study using linked birth/infant death files (2010 to 2013), Wallace et al (2017) identified MSA-level characteristics associated with elevated risk of Black IM, using data on Black IM in 100 U.S. MSAs with the highest Black IM rates.[42] Selection of indicators (Table 18) was guided by data availability at the county or MSA-level, and empirical evidence of bi-variable association between an index and Black IM.

The association between each of the indices and Black IM was estimated separately in a model that accounted for clustering by MSA and included a variable for poverty. Each indicator was at least marginally associated with risk of Black IM. Of particular relevance to individual-level interventions are the 20% and 16% elevation in risk associated with smoking and obesity respectively. These are the two highest risk factors for IM. Also of note are variables that have not been considered in any of the other works reviewed here: mental and physical health days, access to healthy foods and exposure to air pollution (Table 18).

Table 18. Associations between social indices of structural racism and Black infant mortality rates – 100 US MSAs (2010–2013) [1,2,3]

	Black Infant Mortality
	RR (95% CI)
Black unemployment	**1.06 (1.01 1.1)**
Black less than high school education	1.05 (0.95 1.17)
Racial income inequality	**1.08 (1.01 1.16)**
Residential segregation (isolation)	**1.10 (1.05 1.15)**
Smoking prevalence among adults	**1.20 (1.13 1.27)**
Obesity prevalence among adults	**1.16 (1.10 1.22)**
Limited access to healthy foods	**1.09 (1.01 1.19)**
Homicide rate	1.07 (0.99 1.15)
Air pollution	**1.11 (1.03 1.19)**
Jail admission rate	1.06 (0.96 1.18)

Poor mental health days	**1.12 (1.04 1.20)**
Poor physical health days	**1.13 (1.03 1.25)**

[1] Wallace et al (2017)
[2]Each indicator was modeled separately; models accounted for observations clustered within MSA and adjusted for poverty rate in each MSA.
[2] Estimates are the rate ratio comparing NH Black infant mortality rates across an interquartile range increase in the indicator

Discussion

As mentioned above, there are a myriad of challenges in estimating direct and indirect effects of structural racism, and its mediating effects, on risk of IM. Two ecologic studies, by Shaw et al. and Hearst et al. that did not consider individual-level factors, yielded null findings. The hierarchical study by Shaw also yielded null results. Among the few studies included within the limited scope of this review, the evidence directly linking residence in segregated areas with the risk of IM is not strong. On the other hand, fairly consistent evidence links segregation with causes of IM, and there is also evidence of a link between proxies for structural racism, such as prevalence of Black unemployment, and prevalence of mortality among Black infants. However, it remains that the strongest effect estimates were for individual-level risks, particularly smoking and obesity.

Income inequality

Income inequality is a key structural feature of communities and a robust determinant of access to health promoting resources. It has been argued that the evidence linking income inequality and poor health meets epidemiologic criteria for causality.[43] This notion is supported by experimental evidence that health outcomes can be improved through manipulation of levels of income inequality in communities.[44] However, the majority of studies of income inequality have focused on health outcomes other than IM. Below we review the recent literature examining the link between income inequality and IM, including causes of IM among Black populations in the US.

Kramer and Hogue (2008) examined the association income inequality (i.e., the Gini coefficient) and risk of a very preterm birth, using U.S. Linked Birth and Infant Death Data (2002–2004) across 168 MSAs with adequate (not defined) numbers of Black residents to allow stable estimates.[37] Among this sample, income inequality did not predict risk of poor birth outcomes independently of metropolitan population, census region, prevalence of college educated adults and median household income.

In contrast to Kramer and Hogue (2008) who identified MSAs based on qualifying a minimum number of Black residents, Wallace et al.,[42] maximized statistical power of their study by focusing on MSAs with the highest mortality rates for Black infants (reviewed in the previous section, Table 19). In their hierarchical analysis, the authors found a modest positive association between Black income inequality and risk of IM among Black infants (OR 1.08, 95% CI 1.01 1.16) independently of poverty rates in each jurisdiction. The studies below analyzed state-level data, and it has been suggested that the effect of income inequality is most apparent at this level of analysis.

Kershenbaum et al. (2014) examined the association between state-level income and income inequality (i.e., the Gini coefficient) and Black IM across all 50 U.S. states and District of Columbia, using data from the U.S. linked infant birth/infant files (Table 20).[45] This study found a null association between income inequality and Black IM after controlling for the effect of states' median household income as well as poverty. Race-specific Gini measures were not used in these analyses as the authors argued that income inequality in the whole population is most relevant to the study's research question. This perspective, however, is not widely held; evidence suggests the importance of considering race-specific measures of social inequalities.[33,40,41]

Among this Black population, there was a significant association between income inequality and total IMR, but this association is not statistically significant in the case of race specific IMR. The authors concluded that the association between income inequality and IMR is 'complicated by race'. Indeed, it is an aim of this body of work to disentangle this complexity; a more nuanced consideration of race via inclusion of race-specific Gini scores could have helped in this regard (for example, see Wallace et al. 2017). Another shortcoming of this work regards parametrization of the Gini coefficient as a continuous rather than a categorical variable, thus, modeling too small, arguably meaningless, incremental changes in income inequality that require exceedingly high statistical power to estimate.

Table 19. Association between state-level income inequality among Black infants, poverty and IM – US states and District of Columbia (2007-2009) [1,2]

	Black IMR
	r (p-value)
Income inequality	0.15 (.293)
Median household income	
Black	**–0.686 (<.001)**
White	**–0.778 (<.001)**
% living below poverty	
Black	**0.585 (<.001)**
White	**0.762 (<.001)**

[1] Kershenbaum et al. (2014)
[2] Model does not include other variables

Siddiqi et al. (2016) conducted the most detailed analyses of the link between income inequality (the Gini coefficient) and Black IM using U.S. linked infant birth and death records (1992-2007) for 43 states.[46] Seven states (Idaho, Montana, New Hampshire, North Dakota, South Dakota, Vermont, and Wyoming) were excluded from the analytic sample due to having <20 Black IM annually. The authors modeled contemporaneous income inequality and then added to the model variables for lagged income inequality in one-year increments until the effect of income inequality was no longer significant. Among the population included in this study, state-level income inequality and Black IMR were *negatively* associated (ß -0.27 SE =0.07, p <0.01) in bivariate analysis, but in adjusted models, the effect of income inequality became non-significant (ß -0.10 SE=0.07, p=0.16). Inclusion of a two-year lagged effect for income inequality rendered an independent *negative* lagged effect for Black IM (ß -0.159 (SE=0.07; p= 0.02). Median income poverty and other indices of individual-level and state-level economic well-being were also accounted for (Table 20).

Table 20. Associations between state-level income inequality and Black IMR – 43 US states (1992-2007)[1]

	Crude Model	Adjusted Model[2]	Model w. Lagged[2] effects
	ß (SE), p-value	ß (SE), p-value	ß (SE), p-value
Income inequality	-0.27 (0.07), <0.01	-0.10 (0.07), 0.16	-0.09 (0.07), 0.16
1 yr. lagged inc. ineq.	--	--	-0.07 (0.07), 0.28
2 yr. lagged inc. ineq.	--	--	-0.16 (0.07), 0.02
Poverty	--	0.16 (0.09), 0.07	0.12 (0.08), 0.15

[1] Siddiqi et al. (2016)

[2]Model includes: Year of survey, proportion of high school graduates, median income and unemployment rate and variables for within state variation in income inequality.

The authors suggest that one explanation for the observed negative association between income inequality and two-year lagged Black IMR is that 'changes in income inequality represent changes within the context of steadily higher Black income, outpaced by even greater gains to White income. Put differently, the effect of income inequality may depend heavily on how, and in which racial

groups, income is changing.' A burgeoning literature supports the notion that the effect of income inequality is race specific.[34,47]

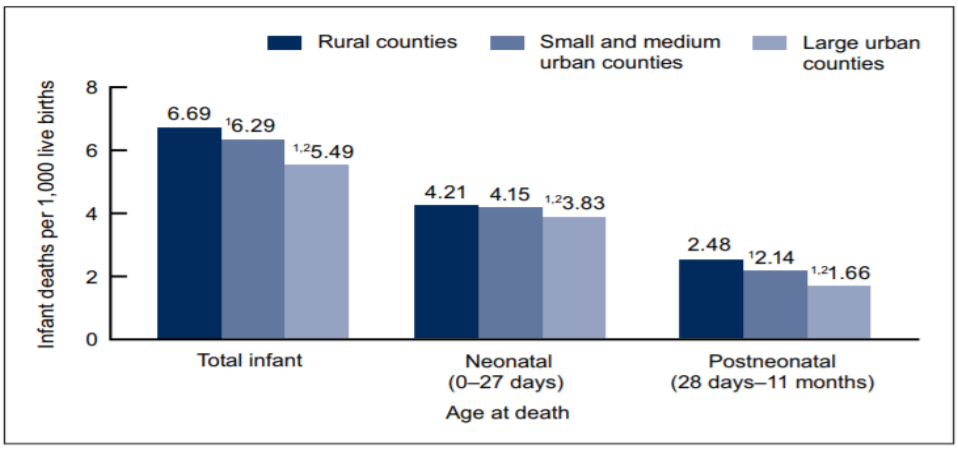
Discussion

The many methodologic approaches within the limited scope of this review highlight the nuanced considerations necessary to consider, and the folly of, making sweeping statements about the health effects of income inequality. With this caveat in mind, it can be said that the reviewed evidence is generally supportive of existence of a modest association between income inequality and risk of infant mortality. The literature reviewed above, and other works outside the scope of this review, also support the relevance of race-specific measures of income inequality, especially when considering race-specific health outcomes. Furthermore, while the study of income inequality is of immense relevance for better understanding the influence of distal determinants (i.e., state and national-level economic and health policies) on the risk of IM, the relevance of this work for informing immediate interventions at the State-level is arguably limited. Within this limit, a conclusion that may be allowed from the reviewed work, one that is also supported by literature outside of the scope of this review, is that income transfer programs, such as Medicaid, can blunt the deleterious effects of income inequality on poor health outcomes.[48] This benefit is likely to extend to risk of IM among Black populations.

Residence in rural areas

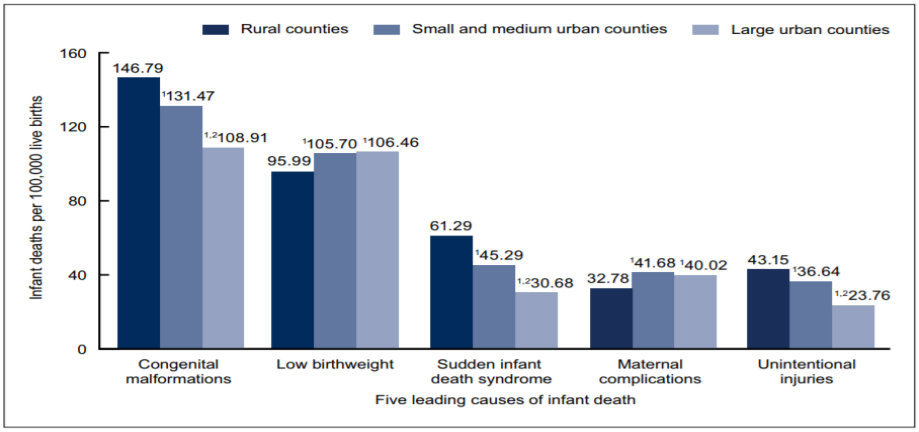
According to the National Center for Health Statistics, during 2013–2015, rural counties had the highest IM rate (6.69/ 1,000 live births), neonatal mortality (4.21/ 1,000 live births) and postneonatal mortality (2.48/ 1,000) (Figure 3).[49] Of the five recognized causes of mortality, rural counties had the highest rates of congenital malformations (147/1000), SIDS (61/1000) and unintentional injuries (43/1000), but had the lowest rates of low birth weight (96/1000) and maternal complications (33/1000) (Figure 4).

Figure 3. Total infant, neonatal and postneonatal mortality rates by urbanizations levels – US (2013-2015)



[1]Significantly different from rural counties ($p < 0.05$).
[2]Significantly different from small and medium urban counties ($p < 0.05$).
NOTES: County designation is based on mother's county of residence as reported on the birth certificate.
County classification is based on the 2013 NCHS Urban–Rural Classification Scheme for Counties.
Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db300_table.pdf#1.
SOURCE: NCHS, National Vital Statistics System, linked birth/infant death data set.

Figure 4. Infant mortality rates for the five leading causes of IM by urbanization levels –US (2013-2015)



[1]Significantly different from rural counties ($p < 0.05$).
[2]Significantly different from small and medium urban counties ($p < 0.05$).
NOTES: County designation is based on mother's county of residence as reported on the birth certificate. County classification is based on the 2013 NCHS Urban–Rural Classification Scheme for Counties. Access data table for Figure 2 at: https://www.cdc.gov/nchs/data/databriefs/db300_table.pdf#2.
SOURCE: NCHS, National Vital Statistics System, linked birth/infant death data set.

The current rural-urban disparity has been persistent. Vital statistics data (Table 21) show disparities in prenatal care utilization and IM, spanning 1985 to 1997.[50]

Table 21. Adjusted odds ratios for risk of select outcomes comparing rural to urban residents – US (1985-2007)

	1985-1987	1989-1991	1995-1997
Poor birth outcome			
Low birthweight*	1.002 (0.994,1.010)	1.037 (1.031,1.043)	1.089 (1.082,1.095)
Neonatal mortality*	1.018 (0.996,1.040)	1.042 (1.019,1.068)	1.174 (1.144,1.204)
Postneonatal mortality*	1.105 (1.077,1.134)	1.173 (1.143,1.203)	1.193 (1.157,1.232)
Inadequate prenatal care (PNC)			
3rd trimester PNC or no PNC*	1.026 (1.021,1.029)	1.038 (1.034,1.042)	1.085 (1.081,1.090)
Inadequate PNC by Kotelchuck index*	1.030 (1.025,1.039)	0.956 (0.950,0.962)	1.035 (1.027,1.043)

* Control variables: maternal race (African American, Native American, other race), maternal age (under 18, over 35), parity (parity = 0, parity > 4), marital status (single), less than 12 years of education (for women over age 18), late prenatal care.

We also note rural-urban disparities in children's health, which very likely mirror similar disparities among infants. According to the National Children's Health Survey, which includes a nationally-representative sample of parent-reported information (Table 21),[51] rural children are more likely than urban children to live in a household with income below the Federal Poverty Level (FPL). While at least 80% of rural children are reported to be in good or excellent health, Black children in rural areas are less likely to report good health than their counterparts in urban areas. A higher proportion of children in rural areas utilize Medicaid or the Children's Health Insurance Program (CHIP) compared with their urban counterparts (Table 22).[51]

Table 22. Select demographic and health indicators by geographic region for children (birth to 17 years) in the United States, 2007

Health/Demographic Indicator	Urban area[1]	Large rural area[2]	Small rural area[3]
Children living below FPL	17%	23%	24%
Children living at or above 400% FPL	33%	17%	14%
Black children reporting good/excellent heath	81%	77%	73%*
Ever breastfed	77%	70%	68%
Ever breastfed and living below FPL	69%	52%*	56%
Overweight or Obese	31%	35%	35%
Live with a someone who smokes	24%	33%	35%
Poor neighborhood conditions[4]	28%	32%	34%*
Received preventive health visit in last year	89%	86%	86%
Received annual preventive health living >400% FPL	92%	88%	85%*

[1] Include metropolitan areas and surrounding towns from which commuters flow into an urban area, including suburban and less densely populated areas.

[2] Include large towns ("micropolitan" areas) with populations of 10,000 to 49,999 persons and their surrounding areas.

[3] Include small towns with populations of 2,500 to 9,999 persons and their surrounding areas.

[4] Defined as living in a neighborhood with garbage on the sidewalk or streets, a high proportion of dilapidated housing, or vandalism

Results for both large and small rural areas were statistically different from urban areas (level of significance not reported), except where indicated; *indicates only small or large area was statistically different from urban area

Regardless of race, rural children (ages 0-5) may be at higher risk for infant mortality on two health indicators associated with postneonatal mortality. Namely, a lower proportion of rural children (68%) are ever breastfed in comparison to urban children (77%). This lower likelihood of breastfeeding initiation is compounded by living in poverty, where only half of rural children living below the FPL are ever breastfed, in comparison to 69% of urban children. Among all children, the lowest prevalence of breastfeeding was observed among Black children living in rural areas (33%). Rural children (36%) are also more likely to live with a smoker than urban children (25%) irrespective of race.

Some risks that are prevalent among children residing in rural areas are likely the same risks as those faced by rural infants. For example, children living in rural areas are more likely than urban children to reside in neighborhoods with poor conditions (i.e., garbage strewn about, many dilapidated homes, vandalism). Children living in rural areas are also slightly less likely than urban children to have preventive health care, this is even true of rural children in the highest income brackets (>400% FPL) irrespective of race. It is reasonable to assume that compared to urban infants, rural infants are more likely to reside in neighborhoods with poor conditions and to not receive as much preventive health care.

There are, however, several protective factors associated with living in rural areas. Children in small rural areas were more likely to share a meal with their parents (51%), attend religious services (58%), and participate in physical activity (34%). For children living below the FPL, a higher proportion of rural children are reported to live in a supportive and safe neighborhood, though this advantage levels off across geographic regions as household income increases beyond 200% FPL.[51]

Harris et al. (2015), using PRAMS data (2000-2011), found that rural residents of Maine, with the exception of prenatal care and birth outcomes (i.e., cesarean section, premature birth, and low birth weight), fared worse on maternal and child health indicators than residents of urban areas.[52] Rural mothers were more likely to be teenagers (10.5% vs. 6.2%), have less than a high school education (51.8% vs. 37.7%), live in a household with annual income below $20,000 (39.6% vs. 28.8%), less likely to be married (66.4% vs. 58%), have higher BMI prior to pregnancy (26.1 vs. 25.3) and were more likely to smoke prior to (35.4% vs. 28.5%) and during pregnancy (22.3% vs. 14.7%). Infants born to women living in rural areas were also less likely to be breastfed for at least eight weeks than those living in urban areas (52.9% vs. 60.9%).

While birth outcomes between rural and urban regions were similar in Maine, widening disparities in infant mortality have been observed on a national level.[53] Appalachia, a region that encompasses rural areas from New York to Mississippi, has generally had a similar rate of IM as the U.

S., with similar declines between 1990-2013, when a gap in the rate began to develop in 1993 as the rate became increasingly higher in Appalachia in comparison to the rest of the U.S. By 2009-2013, the rate of IM in Appalachia was 16% higher than the rest of the U.S. (7.08 vs. 6.10). Among White women, IM was 23% higher in Appalachia by 2009-2013, and for Black women, it was 9% higher. Women living in high poverty areas had higher rates of IM than those living in low poverty areas (55% vs. 39%), regardless of where they lived (Appalachia vs. rest of the U.S.). Given the heterogeneity of the Appalachian region, the authors speculate that these effects may be an underestimate of disparities in rural-urban differences.

McElroy et al. (2012) reported on the prevalence of neonatal and infant mortality among a Missouri population of low-income, rural mothers who participated in two randomized smoking cessation trials (N=993).[54] The prevalence of perinatal mortality rate (fetal deaths at >20 weeks' gestation plus neonatal deaths) among these women was 15.9 per 1000 births (95% CI 7.4–28.1). When considering all intrauterine fetal deaths regardless of gestational age plus neonatal deaths, prevalence of mortality was 50.8 per 1000 births (95% CI, 35.2–70.6). The small numbers, as reflected in the unstable point estimates, limit their interpretability and generalizability to Maryland populations.

Sparks et al (2009) examined differences in determinants of IM rates across U.S. counties (N= 2,935) by degree of rurality, using U.S. mortality data (1998-2002) and U.S. Census of Population and Housing (1990), County Business Patterns (1990), Area Resource File (1990), Uniform Crime Reports (1990) and Toxic Release Inventory (1990).[55] Counties were categorized based on the Urban Institute's classification of urbanity code (1993) which considers proximity to metropolitan counties, size of adjacent counties and number of residents within the county under consideration (Table 23).

In accord with national estimates reported above, with few exceptions, unadjusted models (bivariate model for neonatal death, Table 24) revealed higher risks of neonatal mortality in more rural counties, particularly among counties not adjacent to a city or town. For postneonatal deaths, the unadjusted elevated risk of IM among rural counties extended to almost all rural counties, with only one exception (bivariate model for postneonatal death). However, in models adjusted for socioeconomic status, environmental risks, and health care, the associations between rurality and neonatal mortality *reversed*, with residence in rural counties protective of neonatal mortality. Therefore, with the exception of the most rural areas, this evidence suggests that elevated risk of neonatal mortality observed in rural areas is attributable to factors other than population size and proximity to cities (see below for details). We also note that because Sparks et al did not conduct formal mediation analyses,

future replications of their work that conduct more formal analyses may yield somewhat different results.

Table 23. Associations between rurality, neonatal and postneonatal mortality - US Counties (1998–2002)[1,2]

	Mortality			
	Neonatal		Postneonatal	
	B[3]	A[4]	B[3]	A[4]
	ß		ß	
Metropolitan counties				
≥1million residents	Ref	Ref	Ref	Ref
<1 million residents	**0.37***	0.07	**0.46***	0.04
Nonmetropolitan counties				
Adjacent to large metro counties:				
contains a city of ≥10,000 residents	−0.23	**−0.65***	**0.40***	-.050
no city of ≥10,000	**0.65***	0.010	0.24	-0.21
Adjacent to small metro counties:				
contains a city of ≥10,000	**0.65***	−0.02	**0.32***	**−0.23***
no city of ≥10,000	**0.38***	**−0.31***	**0.61***	0.06
Not Adjacent to small metro counties:				
contains a city of ≥10,000	0.23	**−0.43***	**0.79***	**0.19***
contains a town of 2,500–9,999	0.15	**−0.55***	**0.84***	**0.21***
no town of 2,500–9,999	**0.74***	−0.08	**1.31***	**0.65***

* p<05

[1] Sparks et al (2009)

[2]Multivariable, weighted least-squares regression models

[3] **B**ivariate mode model includes only a measure for rurality

[4] **A**djusted model includes variables for income inequality, county-level SES, social capital, structural disadvantage, health care availability, public infrastructure, environmental concerns, old urban factors, suburban factors

For postneonatal mortality, the risk associated with residence in rural counties not adjacent to a metro county was greatly reduced but remained positive and significant. Residence in a rural area adjacent to a city of ≥10,000 became protective. These findings highlight the importance of proximity to cities that presumably have better hospitals and highlight the distinctions between risk profiles for neonatal and postneonatal mortality among rural infants.

When considering these other social and environmental risk factors, it is important to note that, while in this study by Sparks et al. income inequality was not associated with risk of neonatal mortality, counties with higher unemployment rates and larger proportions of Black residents had higher neonatal mortality rates, emphasizing the role of structural disadvantage in IM. Furthermore, there were inconsistent associations between availability of healthcare resources and neonatal mortality. Having a high number of OB/GYNs and pediatricians was associated with a higher and lower neonatal mortality

rate, respectively. A higher Black neonatal mortality rate was observed in counties with neonatal intensive care units, which may suggest a high concentration of infants in the poorest health accessing these facilities for treatment. Risk factors for high postneonatal mortality included high income inequality and higher structural disadvantage (i.e., high unemployment, high percentage of Black residents). Higher church membership protected against postneonatal mortality among Black populations. Finally, there were few associations between health care resources and mortality, though, like neonatal mortality, postneonatal mortality was slightly higher in counties with the presence of NICUs.

In the most detailed study to date, Mohamoud et al. (2019) conducted a hierarchical analysis to examine the association between county-level rurality and poverty with risk of IM, using U.S. birth-infant death (2013) for U.S. counties in 40 states, representing 2,551,828 births in 2778 counties.[56] Counties were categorized into six categories based on National Center for Health Statistics (NCHS) urban-rural classification (see table 24 from Sparks), and as low (<10%), medium (10-19.9%) and high (>20%) poverty (Table 24).

Table 24. Associations between county- and individual-level predictors of IM – US (20123)[1,2,3]

	Bivariate	County vars.	County + Indiv vars.
	OR (95% CI)	OR (95% CI)	OR (95% CI)
County			
Large central metro	**1.07 (0.93, 1.22)**	**0.85 (0.75, 0.96)**	0.98 (0.9, 1.1)
Large fringe metro	Ref	Ref	Ref
Medium metro	**1.30 (1.18, 1.46)**	1.02 (0.91, 1.15)	1.05 (0.95, 1.17)
Small metro	**1.23 (1.08, 1.41**	0.97 (0.84, 1.10)	0.95 (0.83, 1.08)
Micropolitan (non-metro)	**1.55 (1.37, 1.76)**	**1.19 (1.04, 1.35)**	1.10 (0.97, 1.24)
Non-core (non-metro)	**1.72 (1.51, 1.97)**	**1.31 (1.14, 1.50)**	**1.16 (1.02, 1.33)**
Poverty			
Low	Ref	Ref	Ref
Medium	**1.41 (1.19, 1.66)**	**1.39 (1.17, 1.64)**	1.16 (0.99, 1.36)
High	**1.84 (1.56, 2.18)**	**1.90 (1.60, 2.27)**	**1.31 (1.11, 1.54)**

[1] Mohamoud et al. 2019

[2]Models include maternal characteristics: age, education, race ethnicity pregnancy complications, chronic diabetes tobacco use as well as gestational age.

[2] Hierarchical logistic regression model, individual-level variables nested within counties.

Bivariate analysis revealed that both urban-rural distinction and poverty predict IM. However, considering both of these county-level variables simultaneously rendered null values for counties classified in the middle categories of the urban-rural continuum, such that an elevated risk was observed in the two most rural areas (relative to large metro areas). Once individual-level variables were considered, the marginally significant risk in micropolitan counties was rendered null (OR 1.10, 95% CI: 0.97, 1.24), but a modest 16% (95% CI: 1.02, 1.33) elevated risk remained in the most rural (i.e., non-core) counties. In contrast, adjusting for county urban-rural distinction did not result in a meaningful change in the association between county-level poverty and risk of IM. Inclusion of individual-level factors rendered a null value for the risk associated with residence in medium poverty counties, but a 31% (95% CI 1.11, 1.54) risk remained for residence in counties with high poverty.

Among the 40 states examined by Mohamoud et al., individual-level heterogeneity appears to be the relatively stronger determinant of IM than county-level rurality, with the exception of the most rural areas. This is supported by the findings of multilevel modeling, in conjunction with evidence that, relative to within-county heterogeneity, the marginal contribution of between-county heterogeneity to the overall variance was small. For the most rural areas, there was a 16% elevated risk of IM in non-core counties (i.e. nonmetropolitan counties outside of MSAs), suggesting a geographic association between rurality and IM in these regions. The 16% (95% CI 1.02, 1.33) elevated risk of IM in non-core counties suggest a geographic association between rurality and IM in these most rural areas.

This work by Mohamoud et al. is also informative in regard to importance of individual-level factors. Any smoking during pregnancy and lack of prenatal care (vs. care begun in the first trimester) conferred a 77% (95% CI 1.63, 1.91) and 209% elevated risk of IM respectively, independently of all other county-level and individual level risks. Being married was protective of IM (OR 0.83, 95% CI 0.78, .089). Black residents of these counties experience a 20% (95% CI 1.11, 1.31) elevated risk independently of all other factors, highlighting the necessity of considering the lived experience of African Americans when considering preventive measures for any health outcome, including infant mortality.

Discussion

Although a formal mediation analysis by Mahomoud would have allowed a more definitive statement, evidence from this study, coupled with evidence from the study by Sparks et al., suggest that, with the exception of the most rural areas, urban-rural differences in the risk of IM are likely mediated through area level socioeconomic differences and individual-level factors. In the most rural

areas, access to proper health care is an important determinant of IM. Otherwise, local economic conditions appear to be the primary determinant of risk of IM. The individual-risk factors noted in this review of rural populations are generally the same as those operating within urban areas, but these risks are likely more prevalent in rural than in urban areas.

CONCLUSIONS

We conducted a narrative review of empirical studies of infant mortality among African American and rural populations. We began by reviewing the literature that addressed individual-level clinical, demographic and behavioral factors (Figure 1, Box 1), this group of studies constituted the majority of the peer-reviewed literature on infant mortality published between 2008 and 2018. In line with a vast literature from earlier decades, and, in particular, HRSA's recent report of the Secretary's Advisory Committee on Infant Mortality,[57] our review confirmed the relevance of the known causes of infant mortality. The reviewed literature was consistent in linking preterm and low birthweight with elevated risk of infant mortality in a dose-response manner.

Beyond the known causes of infant mortality (IM), we identified several clinical risks: obstetric complications, chronic as well as pregnancy-related hypertension and history of a previous stillbirth or IM. Although there are no known biologically plausible pathways linking a previous stillbirth or IM with risk of infant mortality in a subsequent pregnancy, history of previous IM can be a useful indicator of women who would benefit from close monitoring during their pregnancy. In one of the studies of risks for SIDS and accidental suffocations, prenatal and/or postpartum depression evinced a strong association with maternal health behaviors that predict risk of IM. Although this association was examined in only one of the reviewed studies, we emphasize that prevention and treatment of depression is potentially a fruitful point of intervention. This is due to the strength of evidence, outside the purview of this review, which links depression with health behaviors implicated in IM. According to our review, smoking and back to sleep practices are the most prominent of these health behaviors. Moreover, depression is a well-established cause of smoking, and across different samples and study designs, infants of women who smoked during and/or after pregnancy experienced an elevated risk of mortality.

We also identified paternal involvement and adequate prenatal care as factors that protect against risk of IM. Although paternal involvement, as indicated by information on the birth certificate, is a poor measure of the extent and quality of a father's involvement with his infant, the protective effect

of paternal involvement was remarkably consistent across the reviewed literature. Perhaps most relevant to the aims of this review is the very consistent evidence of the protective effect of receiving adequate prenatal care, regardless of whether care was defined according to Kotelchuck, Kessner or time of onset criteria. This evidence emphasizes the importance of care that begins during the first trimester and remains available consistently throughout the pregnancy and extends beyond pregnancy. Prenatal care visits are opportunities for care providers to diagnose and manage clinical conditions, intervene to alleviate behavioral risks (e.g., smoking) and educate mothers on preventive measures such as back to sleep guidelines. Prenatal care programs that provide social support, such as centering programs, can also either alleviate the adverse effects of lacking a partner, or help further involve an existing partner with the care of an infant. Finally, we would be remiss not to mention the importance of vaccination and exclusive breastfeeding for the first six months of life. Although in the present review immunization was not examined as a risk factor and breastfeeding was considered only in the context of SIDS, the critical importance of these two factors for promoting infants' health is incontrovertible.

All these individual-level risks and protective factors also operated among residents of rural areas. The higher prevalence of individual-level risks among rural populations is most apparent in the high prevalence of smokers and relatively lower likelihood of receiving preventive care among residents of rural areas.

A consistent conclusion from the sparse literature on access to care (Figure 1, Box 2) is the critical importance of ready and consistent access to quality care for all women, and especially for women with chronic conditions. A majority of women of all races receive postnatal care and have a doctor's visit in the first week after birth. These visits are opportunities to intervene on multiple levels as outlined in the previous paragraphs. However, of critical concern is that Black women are less likely than White women to receive adequate care regardless of their health condition. We recommend Medicaid to be considered as an avenue toward addressing this disparity. Because most Black mothers use Medicaid to pay for delivery, it can be a viable means of providing health promoting and preventive interventions. In this regard, we highlight previous estimates that Medicaid programs can reduce healthcare costs by millions of dollars by shifting to preventive strategies.[31]

Because individual-level factors do not fully explain the persistent disparities in Black and White infant mortality rates, we also reviewed studies of social factors (Figure 1, Box 2 and 3) and risk of infant mortality. We focused on interpersonal racism, structural racism and income inequality. Within the limited scope of the present review, we did not find strong evidence of a direct link between racism or residence in segregated areas and risk of mortality among Black infants. In contrast, we found evidence

of links between race-specific measures of structural racism (e.g., % Black unemployment) and known causes of infant mortality. The reviewed literature on income inequality, a robust social determinant of access to health promoting resources, pointed to a modest association between income inequality and risk of infant mortality. Evidence outside the purview of the current review suggests that income transfer programs, such as Medicaid, can blunt the deleterious effects of income inequality on poor health outcomes;[48] this benefit is likely to extend to lowering risk of IM among all marginalized population, including Black populations. It is also important to note that among the reviewed studies of social determinants, the strongest effect estimates were for individual-level risks, particularly smoking.

It remains that all the identified risks operate among all race and ethnicity groups and both rural and urban areas but are more prevalent among Black and rural populations. With the exception of the most rural areas, the elevated risk of IM in rural areas is attributable to local economic conditions. In the most rural areas, access to proper health care, including well-functioning NICUs, is an important determinant of IM.

We also note that Black women experience an elevated risk of IM regardless of their risk profile and regardless of whether they live in rural or urban areas. This highlights the importance of considering the lived experience of African Americans when considering preventive measures.[58] In the U.S., even well-educated and high-income African Americans do not realize the same-level of protections against risk of mortality that is conferred to White women with similar levels of education and income.[59] This phenomenon is perhaps most pronounced in case of age where the U-shaped association between maternal age and pregnancy outcomes, including infant mortality, that is observed among the general population, instead approaches a linear association among Black women (evidence from literature not within the purview of this review).[60] In another example regarding income, White women who transcend their parents' low socio-economic status as adults experience a significant decrease in their risk of giving birth to a low birth weight baby, but upwardly mobile Black women do not realize the same reductions in risk.[61]

Infant mortality is a multi-factorial phenomenon, with determinants that include health prior to and during pregnancy, those related to the pregnancy, those associated with the birth and newborn experience, and determinants associated with health during infancy.[56] Approximately 40% of infant deaths are attributable to the recognized causes of infant mortality;[50] the majority of these causes are preventable through ready provision of quality and consistent care that should extend beyond pregnancy. We also acknowledge the critical importance of following the full immunization schedule and breastfeeding.

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