Exploring racial disparity in stillbirth rates through structural racism and methylation of stress-related genes: From systemic to epigenetic

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Abstract

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Problem to be addressed: Stillbirth is a major public health problem. The stillbirth burden is on a par with newborn deaths. The stillbirth rate measures not only a substantial portion of the global and national burden of mortality, but also equity and quality of care for women's and children's health. Reducing the numbers of these deaths requires an understanding of why they occur, yet approximately one-third of stillbirths are unexplained, even in settings with high-quality autopsy and placental examination, while deaths considered to be explained are usually ascribed to single, proximal causes. An important limiting factor for efforts to reduce the large and inequitable stillbirth burden has been insufficient research into conditions that could inform prevention strategies and reduce inequity.[1 2]

Substantial evidence exists for associations between structural racism, maternal stress, and adverse pregnancy outcomes, yet research focusing on stillbirth is sparse, particularly at the ends of the causal spectrum—macro-level structural conditions and mechanisms. Several studies have called for research on possible biological mechanisms by which racism, racism-related stress, and stillbirth may be associated, including epigenetic mechanisms.[3-6] The most recent review of causes of racial disparities in stillbirth rates in the U.S. recommended that researchers take a multi-domain approach, considering not just individual-level risk factors, which have been relatively well-studied, but also upstream factors such as institutional racism, and biological mechanisms such as epigenetic modification.[1]

The objective of this dissertation was to explore evidence that could help to explain persistent racial disparities in stillbirth. The specific aims were:

1. To review the literature on racial disparity in stillbirth rates;
2. To assess whether structural racism can help to explain racial disparity in stillbirth rates in New York City; and
3. To assess whether maternal stress is associated with stillbirth, whether stress is associated with methylation of stress-related genes, whether methylation is associated with stillbirth, and whether there is evidence that methylation of stress-related genes mediates associations between stress and stillbirth.

Materials and methods used: For **Aim 1**, we carried out a scoping review of the literature in five databases (PubMed, Scopus, Cinahl, Embase, PsycInfo) to identify all reports including stillbirth rates stratified by race in the U.S., mapping exposures and effect modifiers ("domains of analysis") and authors' comments on racial disparity in stillbirths ("domains of explanation") into one of eight domains (race, genetic, fetal, maternal, family, community, healthcare system, and structural). We defined Stillbirth Disparity Ratios (SDRs) as the ratio of the stillbirth rate in a racial/ethnic minority group to the stillbirth rate in white individuals. Selected SDRs were extracted from each report, as were all SDRs for Black/white comparisons.

For **Aim 2**, we modelled associations between four measures of structural racism and stillbirth in all non-Hispanic (NH) Black and white singleton births in New York City between 2009 and 2018. Exposures were four Public Use Microdata Area (PUMA)-level measures of structural racism (Indices of Dissimilarity, Isolation, and Concentration at the Extremes (ICE), and an Educational Inequity Ratio) constructed from U.S. Census American Community Survey data. Using multilevel logistic regression, we first tested for interaction between race and

structural racism in relation to stillbirth. For structural racism measures that interacted with race, we estimated odds ratios for stillbirth separately in 221,925 NH Black and 325,058 NH white births. Race-specific models were further stratified by maternal age.

For **Aim 3**, we assessed associations between maternal stressors and stillbirth in 183 non-anomalous full-term singleton births (63 stillbirths and 120 livebirths) from the U.S. Stillbirth Collaborative Research Network. Measuring maternal stress with two hypothesized stressors, an Index of Significant Life Events and an Index of Disadvantage, we assessed associations between maternal stressors and stillbirth in our sample, and then whether maternal stressors and stillbirth were associated with differential methylation of 1,191 CpGs on five stress-related genes (*BDNF*, *FKBP5*, *HSD11B2*, *IGF2*, and *NR3C1).* Finally, we assessed whether methylation mediates associations between stressors and stillbirth.

Conclusions reached: For **Aim 1**, we found 95 reports presenting stillbirth rates stratified by race/ethnicity in the U.S. We found evidence of increased risk of stillbirth in Black as compared to white births in the majority of the 83 reports with the necessary data. Among the 1143 Black-white SDRs that we extracted, the median SDR was 1.67, with 74% of SDRs showing evidence of disparity. Family and community factors, healthcare system factors, and structural factors were commonly used as domains of explanation (20-38% of reports), but rarely (family/community, structural, 4-5%) or never (healthcare system) used in analysis. The most commonly used domains of analysis—fetal and maternal factors including gestational age, maternal age, education, and prenatal care—do not appear able to explain the observed racial disparities. Gaps in the literature include a paucity of studies examining the possible role of health system, community, and structural factors in Black-white disparity in stillbirth rates, and limited data on other types of racial disparities in stillbirth rates, including Hispanic and Native

American births.

For **Aim 2**, we found that structural racism as measured by ICE and Isolation was associated with stillbirth in NH Black but not NH white mothers. This would seem consistent with our hypothesis that structural racism may help to explain racial disparity in stillbirth rates; however, the associations we observed were not in the expected direction. Specifically, NH Black mothers living in PUMAs with a high concentration of privilege had 90% *greater* odds of stillbirth in comparison to those living in PUMAs with a high concentration of disadvantage (ICE quintile 5 vs 1), and NH Black mothers living in PUMAs that were the most isolated had 40% *lower* odds of stillbirth in comparison to those living in PUMAs that were the least isolated (Isolation tertile 3 vs 1). We suggest that while the measures we used (ICE and Isolation) do help to explain the Black-white disparity in stillbirth rates, our results raise questions about the way these measures operationalize structural racism, meriting further investigation.

For **Aim 3**, we found that having two or more vs no items in the Index of Disadvantage ("Disadvantage") was associated with more than fourfold greater odds of stillbirth (95% CI 1.58, 12.93). We found no association between the Index of Significant Life Events and stillbirth. We found that 32 out of 1,191 CpGs on five stress-related genes were differentially methylated with respect to stillbirth, and six CpGs were differentially methylated with respect to Disadvantage. Methylation at two CpGs on *IGF2* and one on *HSD11B2* (cg02097792, cg12283393, and cg19413291, respectively) mediated the association between Disadvantage and stillbirth.

Research on causes is a critical component of stillbirth prevention and reducing the inequitable distribution of this public health burden. Limited understanding of causes at both "ends of the spectrum", from upstream distal factors to mechanisms, has likely contributed to slow progress on prevention.[7 8] This dissertation contributes to science and public health by

providing researchers with data to support new lines of inquiry, e.g., into associations between structural racism and stillbirth, and for methylation as a mechanism of effect, that should help to improve our understanding of causes. Our research may also support health policy makers who now have additional data to illustrate the adverse health outcomes of structural racism in the U.S. Finally, it may help the parents and other family members of stillborn babies who continually seek to understand “why”.

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Acknowledgments

Statement of positionality

I wish to acknowledge two aspects of my identity that are particularly relevant to this dissertation and have undoubtedly affected my work on it. As a white person, I am inherently part of the white-dominated society that created and perpetuates the very structural racism I have investigated. As the mother of a stillborn baby, I bring an insider knowledge of stillbirth. My first son, Wilder Daniel, was stillborn at full-term in 1999, 11 days before he was due. Despite an autopsy and extensive testing, no cause was found for his death. Wilder is the reason for this dissertation.

Land acknowledgement

I acknowledge that throughout the years of my PhD study, I have lived and worked on what I now realize is the unceded land of the Ramapough-Munsee Lenape Nation, whose people are still here.

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For Aim 2: All individual-level data on stillbirths and livebirths were obtained from the New York City Department of Health and Mental Hygiene (DOHMH) under a Data Use Agreement between the DOHMH and Columbia University. Many thanks to the team at the DOHMH, especially Mary Huynh and Berton Freedman, and also Wenhui Li and Ying Sun, for providing the data and patiently answering my many questions. Thanks to U.S. Census staff including Jessica Barnett for quickly and helpfully responding to my requests for help, and thanks to friends and colleagues from Columbia University: Autumn Clemons for help with the forest plot, Jia Guo for answering questions on biostatistics, Natalie Levy for advising me on access to and use of Census data and generally being an awesome epidemiology guru, and Dr John Pamplin for generously spending time with me on discussions about racism and health.

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Dedication

In 1999, my first child, Wilder Daniel, was stillborn at full term, with no cause ever found. I had an uneventful, planned pregnancy. One day at the end of week 38, I noticed that my baby was no longer moving, and went into the hospital to be checked out. I found out that my son was dead in the instant when the ultrasound machine produced only static: no heartbeat. I was sent home by the hospital for the night. The next morning, my induction began. It lasted 24 hours. My water broke 48 hours after learning of my son's death. Following a labor of several hours, I gave birth to my 6 pound, 12 ounce son, at least three days after he had actually died, and 11 days before his due date. We spent a day with him before releasing him to the hospital for an autopsy and genetic testing. One week later, following his cremation, we scattered his ashes. Despite extensive investigation, no cause was ever found for his death.

This dissertation is dedicated to Wilder Daniel Leisher.

Chapter 1: Introduction

1.1 Motivation for the dissertation

1.1.1 What is stillbirth?

Stillbirth is the death before or during birth (antepartum, AP, and intrapartum, IP, respectively) of a fetus or baby. There is no globally accepted definition of stillbirth; one study found 34 definitions in use.[9] The World Health Organization (WHO) defines stillbirth as death before or during birth from a gestational age (GA) of 28 weeks on,[10] but many high-income countries count stillbirths from 20 gestational weeks on.[9] In the U.S., although the Centers for Disease Control and Prevention defines stillbirth as fetal death from 20 gestational weeks on, states effectively define stillbirth differently due to different reporting requirements for these deaths,[11] ranging from 16+ weeks' gestation (Pennsylvania) and 350 g+ birthweight (Kansas) to 20+ weeks' gestation (25 states).[12]

Stillbirth is just one of the possible outcomes of conception (Figure 1). Newborn or neonatal deaths are deaths after live birth, including early neonatal death (birth to day 6) and late neonatal death (day 7 to 28). Together, stillbirths and newborn deaths are often referred to as perinatal deaths.[2] While it may seem simple to tell the difference between a livebirth and a stillbirth, misclassification between stillbirths and newborn deaths is a well-known challenge of stillbirth epidemiology. Distinguishing between stillbirths and newborn deaths is complicated by many factors, including differences in definitions of livebirth and stillbirth, insufficient knowledge or training of individuals reporting on birth, local languages that do not distinguish between stillbirth and neonatal death, differences in methods of ascertainment of life and death, and deliberate misreporting related to emotional, financial, administrative, cultural and legal

considerations, all of which may sometimes lead to misclassification between stillbirths and newborn deaths,[13-15] including in high-income settings such as the U.S.[11 16-18]

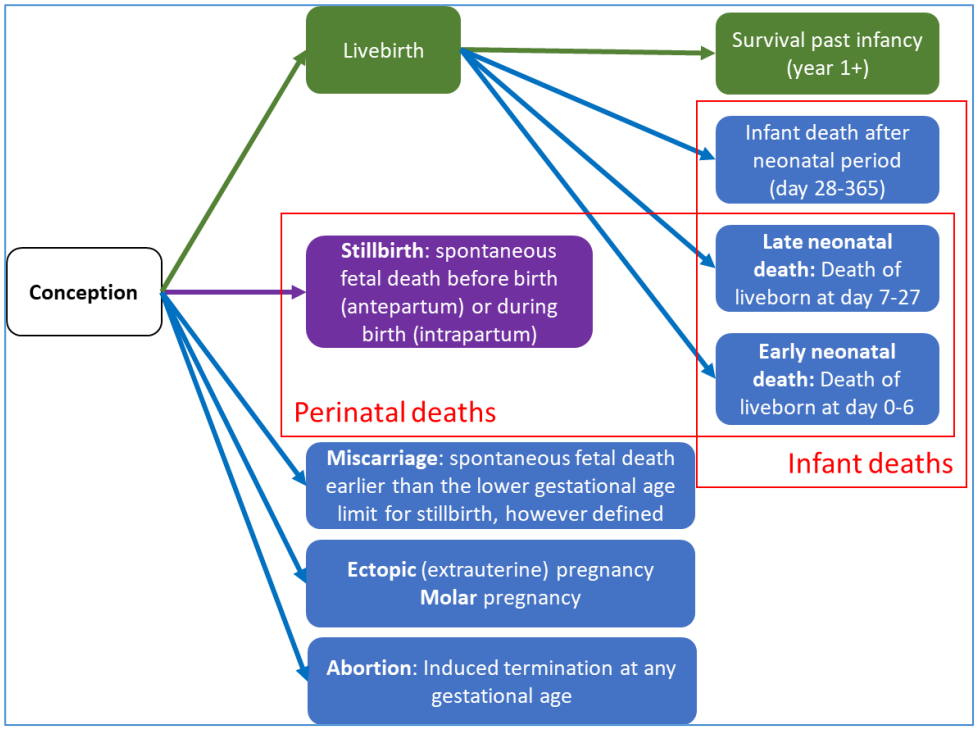

Figure 1: The relationship between stillbirth and other possible outcomes of conception

1.1.2 Why is stillbirth important for public health?

Stillbirths are a major component of the mortality burden: There are two million stillbirths each year, yielding a global rate of 13.9 per 1000 total births.[10] Stillbirths comprise 35% of the global total of 5.75 million perinatal and neonatal deaths (to day 364 after livebirth) (Figure 2) and 3.4% of all global deaths.[2 19]

Stillbirth is often thought to be an issue only in low- and middle- income countries, and indeed this is where 84% of the global stillbirth burden is borne.[10] However, stillbirth constitutes a major public health burden in many high-income countries as well, including the United States. Using the U.S. Department of Health and Human Service's working definition of stillbirth from

the 20th gestational week on, the U.S. stillbirth rate is 5.7 per 1000 total births,[20] higher than the neonatal death rate of 3.7 per 1000 live births.[21] Stillbirths comprise 50% of the 42,000 deaths of infants and newborns in the U.S.[20-22] There were slightly more stillbirths in the U.S. in 2019 than deaths in children aged 0-14 from the top 5 causes of death for that age group (21,478 stillbirths vs 21,394 deaths aged 0-14 from perinatal-related causes, congenital malformations, accidents, cancer, homicide, and heart disease).[22] Stillbirths greatly outnumbered all deaths to children aged 1-14 in the U.S. in 2019 (21,478 stillbirths vs 9,173 deaths aged 1-14 from all causes).[22] The U.S. stillbirth rate also compares poorly on the global stage. Using the WHO definition of stillbirth (28+ weeks), the U.S. rate is 3.0 per 1000 total births, higher than that of 51% of high-income countries (31 of 61 countries with 2020 stillbirth data).[10]

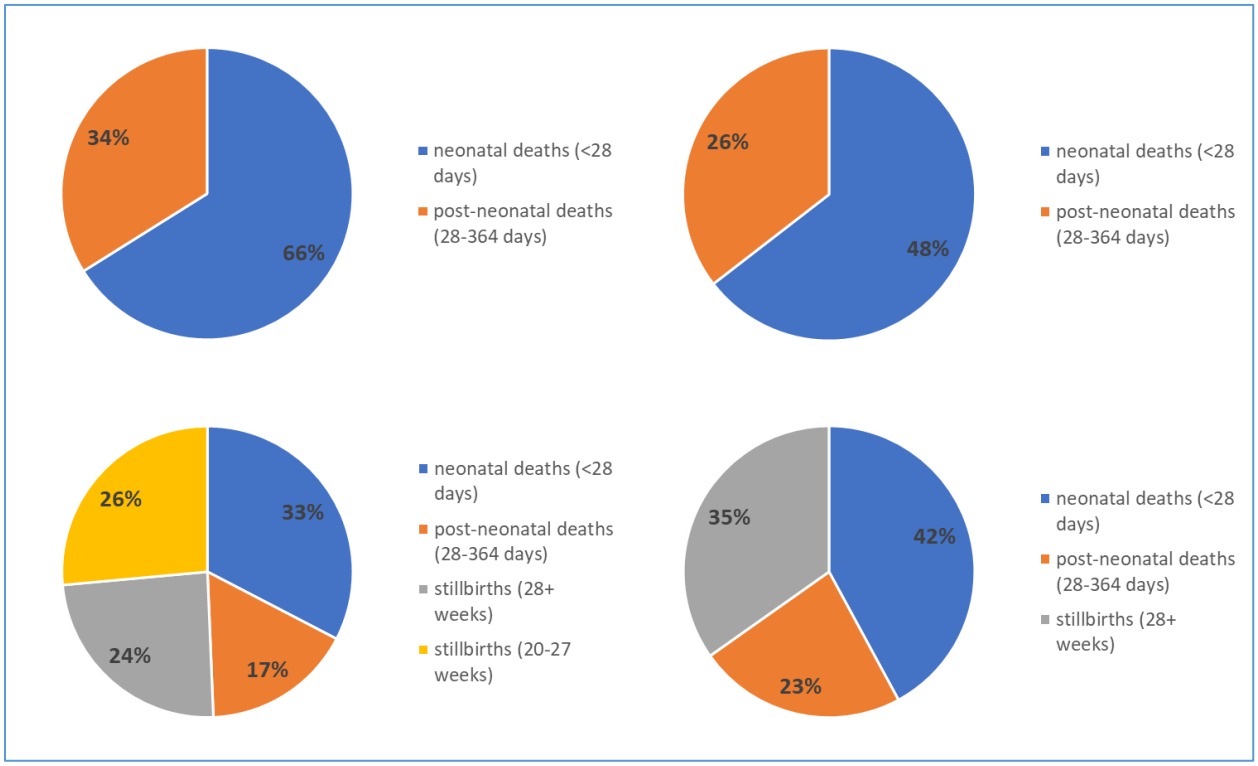

Figure 2: (LEFT) U.S. neonatal and post-neonatal deaths (2019) without stillbirths (top, n=20,927) and with stillbirths (bottom, n=42,405)[20-22]; (RIGHT) Global neonatal and post-neonatal deaths (2019) without stillbirths (top, n=3.75 million) and with stillbirths (bottom, n=5.75 million)[10 19]

The public health burden of stillbirth is multifaceted: The public health burden of stillbirth includes not only death itself but also bereavement associated with death, as well as other associated costs for mothers, other family members, and caregivers.[23] These include financial costs (estimated at 10-70% higher than for livebirths)[24 25] related to autopsy and testing, funeral and burial/cremation, foregone income from work missed, especially if parental leave is not offered for stillbirth or if a parent cannot return to work, and costs related to specialized medical care for subsequent pregnancies; increased risk of mental health problems (estimated at 4.2 million women living with depression after stillbirth)[23], with associated costs for care, if any is available, and if not, going untreated; costs of grief counseling; relationship difficulties; and social isolation, guilt, and disenfranchised grief, exacerbated by the taboo that society places on acknowledging or talking about stillbirth, the lack of legal and workplace recognition for stillbirth, the lack of respectful bereavement care in most settings, and the lack of social recognition of parenthood after stillbirth.[26-43]

Minority and marginalized groups bear the largest share of the stillbirth burden: Marginalized populations are disproportionally represented in stillbirth numbers.[8 44 45] Globally, about two-thirds of stillbirths occur in rural areas with limited access to healthcare,[44 46] and one-third occur in fragile and conflict-affected countries.[a]

Inequity is also a feature of the stillbirth burden in high-income countries, where stillbirth rates are routinely two to three times higher in racial, ethnic, immigrant, low-income, and other minority and marginalized groups than in majority groups, including in the UK,[47 48] New Zealand,[49] Sweden,[50] and Australia.[51] In the U.S., the stillbirth rate in non-Hispanic Black births is more than twice as high as in non-Hispanic white births (10.4 vs 4.7 per 1000 total births),[20] a

[a] Personal communication from Dr Aliki Christou, Institute of Tropical Medicine, Antwerp (5 July 2022).

disparity that has remained unchanged since record-keeping began in 1922 (Figure 3).[1 2] Not only are minority and marginalized groups at higher risk of stillbirth, they also often experience worse care during and after stillbirth.[52-54]

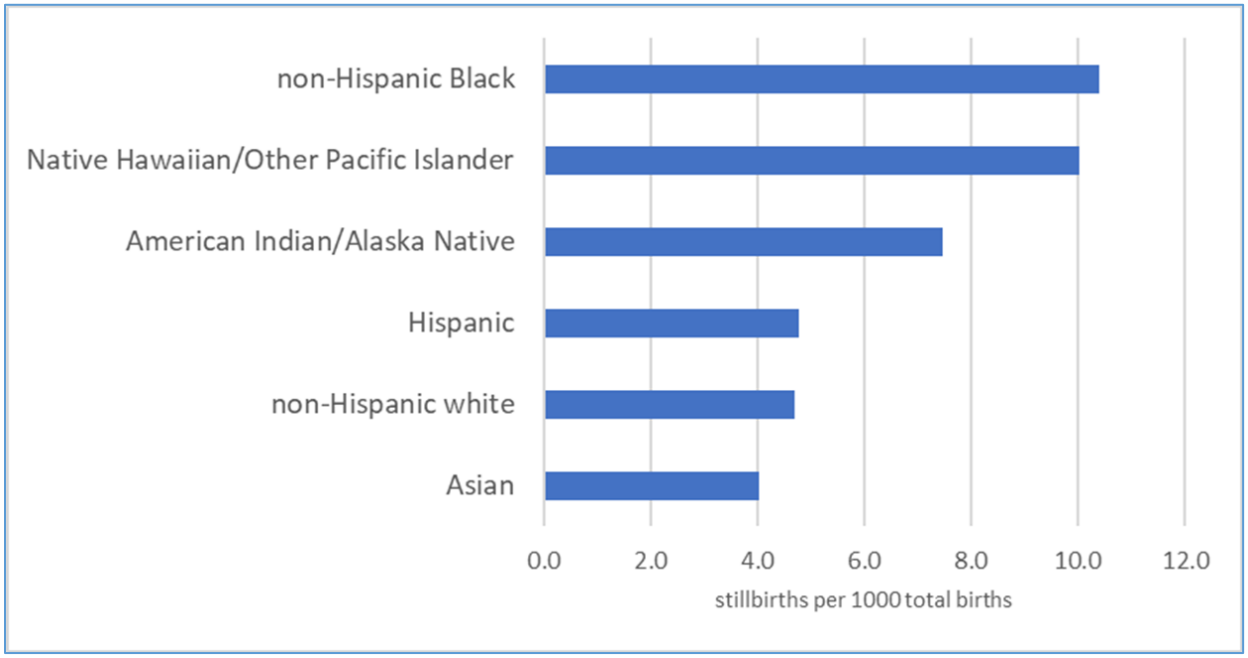

Figure 3: Racial/ethnic disparity in U.S. stillbirth rates, 2019[20]

<u>Most stillbirths are preventable</u>: It is commonly thought that stillbirth is the inevitable loss of a pregnancy 'never meant to be', and relatedly, that most stillbirths are due to unavoidable congenital anomalies.[7] However, a global review found a median of just 7.4% of stillbirths (22+ weeks) could be attributed to congenital anomalies, and even many of these are preventable with interventions such as folic acid supplementation.[44] The majority of stillbirths are considered to be preventable with equitable access to high-quality antenatal and intrapartum care, including comprehensive emergency obstetric care.[27 44] These include most intrapartum stillbirths, which constitute 40% of all stillbirths globally.[10] Other interventions such as prevention or detection and management of syphilis, malaria, diabetes, hypertension, obesity, and fetal growth restriction, facility delivery, and post-term induction could additionally prevent

hundreds of thousands of stillbirths each year.[44 55]

In the U.S. as well, the majority of stillbirths are preventable. Approximately 10% of stillbirths are due to congenital malformations and chromosomal abnormalities.[20] A CDC study estimated that 345-701 neural tube defects (NTDs) in live births could be prevented with increased intake of folic acid supplementation, and it is likely that this would additionally prevent some of the stillbirths due to NTDs.[56] An additional 58% of stillbirths are due to potentially preventable conditions such as maternal complications of pregnancy, complications of the placenta, cord and membranes, maternal conditions unrelated to pregnancy, fetal injury and fetal infection.[20] Additional stillbirths could be prevented with interventions to reduce well-established risk factors for stillbirth such as diabetes, hypertension, smoking and obesity.[8 9 57]

Many studies and national data provide evidence that approximately one-third of global stillbirths are unexplained.[2 9 58-61] In the U.S. as well, 31% of stillbirths are unexplained.[20] This proportion holds even for well-investigated stillbirths; for instance, in the NICHD Stillbirth Collaborative Research Network dataset, created to explore causes of stillbirth, with near-complete investigation and standardized protocols, and using a purpose-built classification system for causes of death, no "probable or possible" cause could be found for 24% of stillbirths.[57] This might seem to imply a natural barrier to stillbirth prevention, since knowledge of causes is key to prevention. However, the wide variation in national stillbirth rates (using the 28+ week WHO definition), from 1.5 per 1000 total births in Japan and 1.9 in Iceland to 32.2 in Guinea-Bissau and 30.6 in Pakistan, demonstrates that very low stillbirth rates are achievable, since there are no known biological differences that could account for the widely differing rates.[10]

1.2 Identifying the research questions

1.2.1 Gaps in thinking about causes of stillbirths

As discussed above, a key characteristic of the stillbirth burden is its inequitable distribution, both between and within countries. Reducing the stillbirth burden both globally and nationally will require action to reduce inequities in stillbirth rates. This in turn requires understanding more about what drives these inequities. Phelan and Link theorized that persistent links between low socioeconomic status and mortality can be explained by underlying systemic inequalities, and that both disadvantage and racism are upstream causes of health inequities; hence, resolution requires structural change.[62 63] Such changes for stillbirth prevention might, on a global basis, include reduced conflict, increased access to high-quality reproductive healthcare, and particularly in the U.S., elimination of structural racism. Indeed, one study estimated that reduced segregation could prevent 16% of all NH Black stillbirths a year.[20 64]

Yet most classification systems for causes of stillbirth conceptualize causes as proximate to death, such as hemorrhage or chorioamnionitis; distal factors such as healthcare quality or poverty are considered separately, if at all. For example, the South African Perinatal Problem Identification Programme records "avoidable factors" such as late initiation of prenatal care separately from cause of death.[65] The usual research paradigm for stillbirths is thus temporally and physically centered on the medically-attended pregnancy, to the exclusion of factors prior to initiation of care or beyond the purview of health workers.[66] Limiting the causal field in this way belies evidence suggesting that distal factors contribute substantially to high rates of stillbirths and disparities in stillbirth rates both between and within countries, as predicted by Phelan and Link's theory of fundamental causes of health inequities.[62]

1.2.2 Looking upstream—structural factors

Rothman's definition of cause—"an event, condition, or characteristic that preceded the disease event and without which the disease event either would not have occurred at all or would not have occurred until some later time"—does not distinguish between proximate and distal conditions and so is consistent with fundamental causes theory.[67] It allows for multiple causes of health outcomes, each sufficient but none required, and multiple components of each causal mechanism, each required but none sufficient. An investigation of plausible upstream causes of stillbirth could not only help to reduce numbers of unexplained deaths, but also shed more light on deaths heretofore considered "explained" by single causes, uncovering new opportunities for prevention.

Consistent with Phelan and Link's theory of fundamental causes, which implicates systemic upstream factors in the persistence of inequity in health outcomes, structural racism is a plausible cause of racial inequities in stillbirth rates in the U.S.[62] Racism may increase the risk of stillbirth disproportionately among racial/ethnic minority groups including Black Americans indirectly, for instance through affecting access to and quality of prenatal healthcare, but also directly, through physiological responses to maternal stress related to racism.

Cohen et al. define psychosocial stress as "occur[ring] when an individual perceives that environmental demands tax or exceed [their] adaptive capacity" ([68], p.1685). Stress can be measured by assessing individuals' perceptions of stress (e.g., through validated questionnaires), individual-level biological responses to stress (e.g., cortisol levels), or group- or individual-level events, processes or conditions hypothesized to create stress (which we define as "stressors"). Stress is distinct from, though can interact with, psychiatric disorders such as clinical depression or PTSD. Stressors can be acute or chronic, range from low-level to severe, and stem from

childhood or range across the lifecourse. Stressors may relate to employment (job loss, job satisfaction), family (number of children, partner support), finances (poverty, income stability), health (chronic pain, worry over medical conditions posing a threat to pregnancy), community (crime rates, crowding), catastrophes (natural or human-made disasters), racism (interpersonal, vicarious), adverse events (domestic violence, abuse), and more.[69] Resources such as resilience and social support can modify the effect of stressors on perceived stress, and coping mechanisms (e.g., smoking, overeating, exercise, substance use) can be both responses to and modifiers of these associations.

There is substantial evidence for a connection between stress and many adverse health outcomes, including pregnancy outcomes such as preterm birth and low birthweight.[68-72] Further, there is some evidence directly linking maternal stress to stillbirth.[68 73] For instance, three U.S. studies found that greater numbers of adverse childhood experiences[74 75] and significant life events[76] were associated with increased odds of stillbirth. Additionally, four large cohort studies in Europe found increased risk of stillbirth to be associated with high perceived stress, bereavement, and unemployment.[77-80] Limitations of these studies included conflation of stillbirths with fetal deaths under 20 weeks and the use of single measures of stress; none looked at biological mechanisms. Only two studies have examined racism and stillbirth. Each found evidence for increased odds of stillbirth with greater levels of segregation, with stronger magnitudes of association in Black than white mothers[64] and in areas with higher segregation.[81] However, neither examined possible mechanisms by which this upstream factor might increase the risk of stillbirth.[64 81]

1.2.3 Looking downstream—mechanisms of action

A causal relationship between stress and adverse pregnancy outcomes is biologically

plausible.[68 73 79 82] Stress works through physiological pathways, including the neuroendocrine, inflammatory, and vascular pathways, as well as via a behavioral pathway.[68] Stress may activate multiple pathways simultaneously or sequentially, and factors on each pathway may interact with each other, or mediate or confound other pathways, leading either directly or via other intermediate adverse outcomes such as infection, preeclampsia and fetal growth restriction, to stillbirth.[69 73 75 83] The placenta is the organ through which all nourishment reaches the fetus, hence the health of the placenta—with a lifespan that ends naturally at birth—helps to determine the health of the fetus. Physiological responses to stress can damage placental functioning and increase inflammation, reducing fetal defenses and compromising fetal health through suboptimal placental development or performance, increasing the risk of stillbirth.[68 69 73 75 78 79 83-87]

Placental dysfunction can be caused by premature placental senescence (ageing due to loss of cellular function), reducing placental capacity to nourish the fetus, related to oxidative damage to DNA that may result from stress.[88-91] Angiogenesis, the development of new blood vessels to ensure proper vascularization of the placenta as fetal development proceeds (as well as proper responsiveness to insults such as hypoxia), is regulated in part by the vascular endothelial growth factor (VEGF) and transforming growth factor (TGF)-β signaling systems which are essential for fetal survival. Placental dysfunction can be caused by changes in the expression of angiogenic and anti-angiogenic factors, affecting placental functioning and thus fetal wellbeing, possibly caused in part by inflammation.[88 92-94] Placental dysfunction may also be characterized by inflammation, which may stem from external stressors. Infection may lead to stillbirth both directly[95 96] and through impaired placental function or abnormal fetal responses to inflammation.[97 98] Stress can reduce the fetal capacity for a proper inflammatory response,[73] with

the impaired response in turn making the fetus more vulnerable to stressors such as infection.[99] Hence, stress may cause stillbirth through physiological impairment of stress responses, increased inflammation and placental dysfunction, and reduced fetal capacity to response to these insults.

An additional possible mechanism by which stress may cause stillbirth is epigenetic silencing through DNA methylation of stress-related genes in placental tissue. Many stress-related genes are highly expressed in the placenta, and epigenetic modification has been associated with adverse prenatal exposures and fetal outcomes.[100] The effect of glucocorticoids in managing the body's proper response to stress is governed in part by genes such as the glucocorticoid receptor gene *NR3C1*, and *HSD11B1* and *HSD11B2;* these genes code for enzymes that provide fetal protection against cortisol.[101] Methylation of these genes may downregulate their expression with possible adverse effects.[100] A systematic review of adverse maternal exposures, perinatal outcomes, and methylation of these three genes found 19 studies, including some which provided evidence that stress may be associated with decreased birthweight via a methylation pathway.[100] However, only two of the studies assessed fetal outcomes, and neither included stillbirth. There has been no research on epigenetic mechanisms as mediators of the pathway from maternal stress to stillbirth.

1.3 Dissertation aims and approach

There are many gaps in research on stillbirth. An important one is in our understanding of causes of racial disparities in stillbirth rates in the U.S. The most recent review in this area recommended that researchers take a multi-domain approach, considering not just individual-level risk factors, which have been relatively well-studied, but also upstream factors such as institutional racism, and biological mechanisms such as epigenetic modification.[1] The objective

of this dissertation was to examine both ends of the causal spectrum for stillbirth—macro-level structural conditions as well as mechanisms—for a better understanding of this gap (Figure 4).

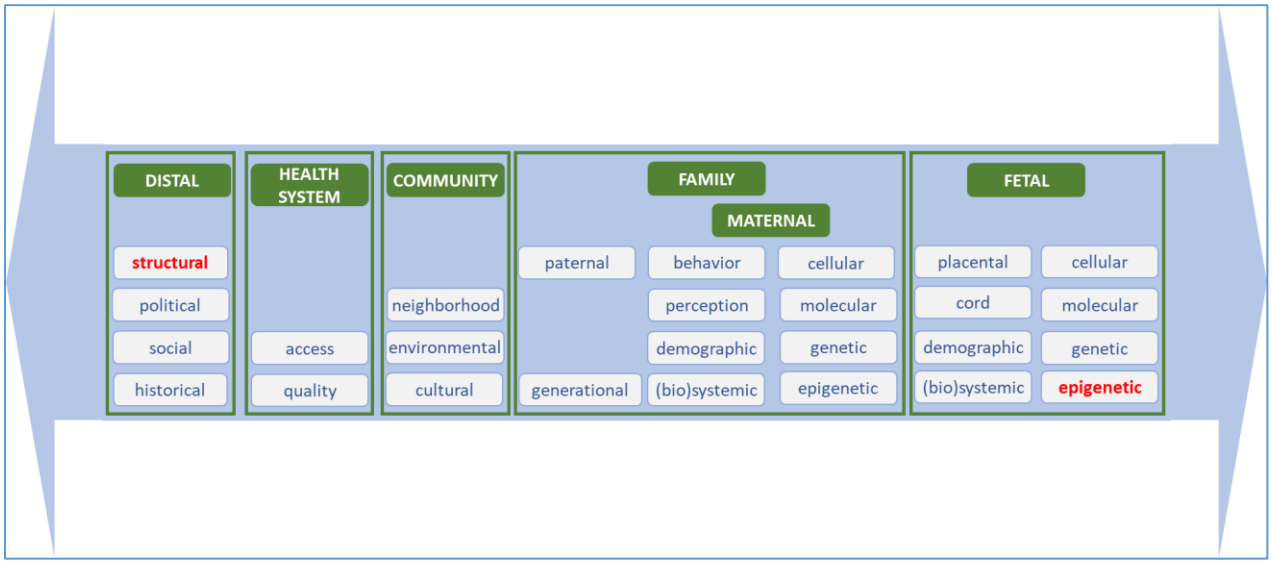

Figure 4: A causal spectrum for stillbirth

The aims of this dissertation were to:

- **Aim 1**: Conduct a scoping review of the literature on racial disparity in stillbirth rates. We aimed to identify all studies that included stillbirth rates stratified by race; subsequently the search was limited to the U.S. Databases searched included PubMed, Scopus, Cinahl, Embase, and PsycInfo. The only limit was English (no date limit). We defined Stillbirth Disparity Ratios (SDRs) as the ratio of the stillbirth rate in a racial/ethnic minority group to the stillbirth rate in white individuals. Selected SDRs were extracted from each included report, as were all SDRs for Black/white comparisons. We categorized exposures and effect modifiers ("domains of analysis") and comments on racial disparity in stillbirths ("domains of explanation") into one of eight domains (race, genetic, fetal, maternal, family, community, healthcare system, and structural), aligned with the proposed causal spectrum for stillbirths (Figure 4).

- **Aim 2**: Assess whether structural racism can help to explain racial disparity in stillbirth rates in New York City. The study population was all 1,077,041 livebirths and stillbirths registered in NYC from 2009 to 2018. Exposures were four Public Use Microdata Area (PUMA)-level measures of structural racism (Indices of Dissimilarity, Isolation, and Concentration at the Extremes, and an Educational Inequity Ratio) constructed from U.S. Census American Community Survey data. Using multilevel logistic regression, we first tested for interaction between race and structural racism in relation to stillbirth. For structural racism measures that interacted with race, we estimated odds ratios for stillbirth separately in 221,925 non-Hispanic (NH) Black and 325,058 NH white births, based on the recognition that structural racism has a different meaning for Black individuals who are oppressed by it, and white individuals who are privileged by it. Race-specific models were further stratified by maternal age.
- **Aim 3**: Assess whether maternal stress is associated with stillbirth, whether stress is associated with placental methylation of stress-related genes, whether placental methylation of stress-related genes is associated with stillbirth, and whether there is evidence of mediation of associations between stress and stillbirth by methylation of stress-related genes. The sample comprised 183 non-anomalous full-term singleton births (63 stillbirths and 120 livebirths) from the population-based U.S. Stillbirth Collaborative Research Network case-control study. Measuring maternal stress with two hypothesized stressors, an Index of Significant Life Events and an Index of Disadvantage, we assessed evidence for associations between maternal stressors and stillbirth. Next, we assessed whether maternal stressors and stillbirth are associated with differential methylation of 1,191 CpGs on five stress-related genes (*BDNF*, *FKBP5*, *HSD11B2*, *IGF2*, and *NR3C1).*

Finally, we assessed evidence for whether methylation mediates associations between stressors and stillbirth.

1.4 Conclusion

Stillbirth has been acknowledged as a major component of "unfinished business" from the Millennium Development Goals, yet was also excluded from the Sustainable Development Goals, launched in 2015.[102] Annual UN country-specific stillbirth estimates were only begun in 2020. Global progress on stillbirth prevention, though it has improved over the past decade, remains too slow to achieve the UN target of 12 stillbirths per 1000 total births by 2030, a target that was endorsed by 194 member nations at the 67th World Health Assembly in 2014.[44]

As with most high-income countries, the U.S. has already met this global target. Indeed, the target was set to be bold yet potentially achievable for the low- and middle-income countries that contribute the largest share of global stillbirths. High-income countries with significantly greater resources for public healthcare should be performing much better than this global benchmark. Yet as mentioned above, the U.S. stillbirth rate is worse than that of 31 other high-income countries, and is twice as high as the lowest rate (in Japan). Moreover, the stillbirth rate in some U.S. minority groups, notably Black Americans, is twice as high as the national rate. Despite this poor performance, in the U.S. as well as globally, there has been limited attention to stillbirths.[2] The CDC's most recent vital statistics report on deaths (2020) excludes stillbirths,[103] and the first report of causes of U.S. stillbirths was only issued in 2016.[61] The U.S. has also reduced the ambition of its national stillbirth rate target; the goal in 2010 was to reduce the stillbirth rate to 4.1 stillbirths per 1000 total births, but in 2020 the goal was revised *upward* to 5.6 per 1000 total births, a *higher* rate than aimed for in 2010.[104 105]

Stillbirth is a major public health problem. The stillbirth burden—both mortality and

post-stillbirth bereavement and follow-on effects for family members and caregivers—is on a par with newborn deaths.[23 26 106-108] The stillbirth rate measures not only a substantial portion of the global and national burden of mortality, but also equity and quality of care for women's and children's health. Reducing the numbers of these deaths requires an understanding of why they occur, yet approximately one-third of stillbirths are unexplained, even in settings with high-quality autopsy and placental examination, while deaths considered to be explained are usually ascribed to single, proximal causes. An important limiting factor for efforts to reduce the large and inequitable stillbirth burden has been insufficient research into conditions that could inform prevention strategies and reduce inequity.[1 2]

Substantial evidence exists for associations between structural racism, maternal stress, and adverse pregnancy outcomes, yet research focusing on stillbirth is sparse, particularly at the ends of the causal spectrum—macro-level structural conditions and mechanisms. Several studies have called for research on possible biological mechanisms by which racism, racism-related stress, and stillbirth may be associated, including epigenetic mechanisms.[3-6] In particular, a 2010 NICHD workshop on stillbirth pointed to racism-related stress as leading to physiological stress responses that may cause racial disparities in preterm birth, and highlighted lack of research on biological mechanisms for how stillbirth occurs.[109]

Stillbirth merits greater attention because of the size of the public health burden that it represents, the inequitable distribution of that burden, its amenability to alleviation, and the insufficient attention that has nonetheless so far been paid to it, both globally and in the U.S. It is hoped that this dissertation will play a role in responding to this research need, contributing to knowledge of preventable causes, highlighting the role of stressors in persistent inequity in stillbirth rates, generating new hypotheses for further study, informing the development of

interventions at individual and policy levels to reduce stillbirth numbers, and helping a little to respond to the needs of bereaved families, thus answering Galea's call for a consequentialist epidemiology.[110]

Chapter 2: Scoping review of the literature on racial disparity in stillbirth rates in the United States

2.1 Introduction

Stillbirth constitutes a substantial public health burden in the U.S., with over 21,000 in utero deaths at 20 or more gestational weeks annually, producing a stillbirth rate of 5.7 per 1000 total births (livebirths and stillbirths) (2019 data).[20] This rate is nearly twice as high as the rate of early neonatal deaths in the U.S. (deaths of liveborn infants at less than 7 days from birth, 3.0 per 1000 livebirths, 2019 data),[111] and using the global definition of stillbirth (fetal death at >28 completed gestational weeks), the U.S. stillbirth rate is higher than that of 51% of high-income countries (31 of 61 countries with 2020 stillbirth data).[10]

Stillbirths occur more frequently in most racial and ethnic minority groups. In the U.S., the stillbirth rate in non-Hispanic (NH) Black families is twice as high as the stillbirth rate in NH white families (10.4 vs 4.7 per 1000 livebirths and stillbirths), with NH Native Hawaiian/Other Pacific Islander and NH American Indian/Alaska Native families also experiencing higher rates of stillbirth than white families (10.0 and 7.5, respectively).[b] While various risk factors that might explain Black-white differences have been identified (e.g., obesity, prenatal care access, gestational age), the doubled risk of stillbirth in Black versus white families has remained constant since U.S. stillbirth data collection began, in 1922.[1]

To date, there has been no systematic review of racial disparities in stillbirth rates, although a 2018 systematic review of pregnancy outcomes in high-risk women in association

[b] Whenever referring to data from a specific report, we used the racial/ethnic group terms that were used in that report.

with short (<18 months) and long (24+ months) interpregnancy intervals (defined as the time between the end of one pregnancy and the start of the next, IPI) did include stillbirth as one of the outcomes. That review found limited evidence that short IPI could help to explain racial disparity in adverse pregnancy outcomes between African-American and white women.[112] A non-systematic review by Hogue and Silver in 2011 summarized the literature on risk factors for stillbirth that are either more common in racial/ethnic minorities or for which there is evidence of stronger adverse associations with stillbirth in these groups.[1] However, none was identified that could potentially explain the doubled risk of stillbirth in Black as compared to white families.

Several non-systematic reviews of racial disparities in perinatal and infant mortality and other related pregnancy outcomes have mentioned stillbirth.[113-116] However, all of these concluded the evidence was insufficient to explain the observed racial disparity, regardless of the exposures assessed. Two systematic reviews of racial disparity in birth outcomes associated with stillbirth (birthweight, gestational age, small-for-gestational age, and preterm birth) also concluded that neither individual- nor area-level socioeconomic status characteristics such as education, poverty, and occupation could explain the disparity; however, neither review mentioned stillbirth.[117] [118] Several non-systematic reviews of racial disparity in birth outcomes associated with stillbirth similarly either did not mention stillbirth or mentioned it only in passing.[5] [119-125]

The most recent review of racial disparity in stillbirth rates was carried out over a decade ago and was not systematic;[1] all other extant reviews on related outcomes have provided limited or no discussion of racial disparity in stillbirth, and several of these have reviewed only specific risk factors (IPI, infection, vitamin D). The aim of the present study was to address these gaps by conducting a scoping review of the literature on racial disparity in stillbirth rates.

2.2 Methods

2.2.1 Study design

This was a scoping review of the literature.

2.2.2 Search

The literature search aimed to identify all reports, regardless of location, of studies that included stillbirth rates stratified by race. Due to the large numbers of reports that passed the first two screening phases, our search was subsequently limited to U.S. only. Search concepts were "stillbirth" and "racial/ethnic disparity" (Table A1). Stillbirth was defined either as (a) defined by the author, or if no definition provided, then as (b) spontaneous loss at 20 or more gestational weeks. Searches were conducted for English-language reports only; there was no date limit. The search was conducted on February 20 and 21, 2021, in five databases: PubMed, Scopus, Cinahl, Embase and PsycInfo. After elimination of duplicates, search results were exported to Covidence.

Screening was performed in Covidence in three phases, with inclusion/exclusion criteria iteratively refined to achieve a reasonable number of reports for full text review. Double full text review was carried out by two epidemiologists (SHL and EL) for 456 reports. All full texts were obtained. The inclusion criterion was any report providing stillbirth rates stratified by race/ethnicity. Exclusion criteria were: live birth only; stillbirth not mentioned, or only as a confounder; stillbirth rates not reported separately from other outcomes or not stratified by race/ethnicity; study sample that only included deaths (hence no denominator data available), or case-control study with stillbirths as cases; stillbirths allowed in study populations but none reported; grey literature (e.g., non-profit reports)[126]; non-U.S.; literature review (though relevant reviews were added to snowball review). We did not exclude studies with overlapping study

populations as doing so would reduce rather than improve our ability to achieve our aim. See Appendix B for more information about the search.

2.2.3 Data extraction

After piloting the data extraction tool, data were double extracted. Due to the volume of work, a third epidemiologist (AC) joined the team at this stage (SHL extracted all 95 studies, EL extracted 54 and AC extracted 43). The data extraction tool was revised throughout the process to improve instructions and adjust data items. Double-extracted data included:

- **Study data**: Study title, authors, year published, aim, design, location, years of included births, population, inclusion/exclusion criteria, data source, exposures, and outcomes. Studies were identified as focusing on stillbirth, racial disparity, both, or neither.
- **Stillbirth definition:** Stillbirth definition, if provided, and whether this could have included fetal deaths <20 weeks.
- **Selected Stillbirth Disparity Ratios**: We defined the Stillbirth Disparity Ratio (SDR) as the ratio of the stillbirth rate in a racial/ethnic minority group to the stillbirth rate in white births[11] (in three cases, a different comparison was used—non-Black, non-Hispanic, and minority).[116 121 125] To keep the workload for double extraction manageable, we aimed to extract a single SDR from every included report—the "**selected SDR**". For reports providing data on multiple racial/ethnic groups, we extracted one SDR for each group. For accuracy's sake, we used the racial/ethnic group terms that were used by authors. If reports provided estimates from regression analysis, we extracted these, along with 95% confidence intervals, the type of estimate (e.g., odds ratio), the exposure, whether estimates were adjusted, and if so, the covariates adjusted for. Where estimates from regression analysis were not provided, we extracted rate ratios (either directly, or

constructed from frequency data). For reports providing multiple estimates for each group (due to stratified analyses or the use of multiple exposures), we developed a rubric to select one (see Appendix B for details). SDRs from duplicated data were not extracted (e.g., government reports that reported national stillbirth data from the same year).

- **Disparity comments**: We extracted and categorized authors' comments on racial/ethnic disparity in stillbirth rates. Comments were extracted from the discussion section of included reports (or from relevant text if there was no discussion section), focusing on authors' views on possible explanations for any racial disparities in the stillbirth data.

In addition to the selected SDRs that were double-extracted, SHL also single-extracted data for all available SDRs that provided Black-white comparisons. Our particular focus on Black/white SDRs was due to the fact that the largest stillbirth rate disparity in the U.S. is between Black and white births.

2.2.4 Analytical approach

Descriptive statistics were produced to summarize the included studies. We reported SDRs and, where possible, their 95% CIs (see Appendix B). For reports presenting regression estimates, if the exposure was race, the SDR equaled the regression estimate for minority vs white stillbirths, hence the 95% CI for the SDR was equal to that estimate's 95% CI; if the exposure was not race, we were unable to calculate the 95% CI for the SDR. For reports presenting stillbirth rates only (no regression estimates) and with either total numbers of births by race or stillbirth numbers by race, we calculated 95% CIs for SDRs; if these data were unavailable, 95% CIs could not be calculated.

We interpreted an SDR greater than 1 (and if 95% CIs were available, with a 95% CI whose lower bound was greater than 1) as indicative of greater risk of stillbirth in racial/ethnic

minority births than in white births (hereafter "**disparity**"), and an SDR less than 1 (and if 95% CIs were available, with a 95% CI whose upper bound was less than 1) as indicative of the reverse (hereafter "**protection**"). SDRs were stratified by racial group comparison, whether 95% CIs were available or not, whether constructed from adjusted estimates or not, and whether there was evidence of disparity, protection, or neither, and median SDRs in each stratum were reported. Following PRISMA guidelines for scoping reviews, we did not perform quality assessment of the included reports.[127]

For Black-White SDRs, we categorized and mapped all exposures and effect modifiers (for SDRs produced from regression estimates) and factors by which rate ratios were stratified (for SDRs produced from rate ratios) to one of eight "**domains of analysis**": race; genetic; fetal (further subdivided into "**categories**" such as gestational age, sex, and birthweight); maternal (including categories such as maternal age, education, stress, and pregnancy health); family; community; healthcare system (including categories such as quality, access); and structural (including categories such as racism). Authors' comments on racial disparity in stillbirths were also mapped to these same domains ("**domains of explanation**"), and domains of analysis and explanation were compared (see Table A2 for details of what the domains included). By design, all reports conceptualized race as either an exposure or an effect modifier, or stratified stillbirth rates by race.

2.2.5 Software

For searches and screening, we used Endnote and Covidence; for data analysis, we used Excel and R.

2.3 Results

2.3.1 Search results

A total of 3,144 reports were identified from five databases (Figure 5, Table A3, Table A4, Table A5, Table A6, Table A7). Of these, 1,220 were duplicates (1,039 found by Endnote or Covidence and 181 by hand review), leaving 1,924 for abstract and title screening. In addition, 470 reports were identified through snowball review. After excluding 1,938 reports, a total of 456 underwent full text review, of which 95 were included (Table A8).

Eighty-eight reports had data allowing presentation of SDRs using the white stillbirth risk as the denominator. (Four reports found no stillbirths in white mothers, so SDRs using the white stillbirth risk as the denominator could not be calculated[128-131]; two reports used non-Black and non-Hispanic as references for Black and Hispanic stillbirth rates, respectively[132 133]; and one report used the "minority" stillbirth rate as a reference for the white stillbirth rate[134]). Black-white SDRs were extracted from 84 reports and SDRs for other racial/ethnic minority groups were extracted from 52 reports. One report was excluded from SDR reporting as its SDR data were duplicated in other reports, but it was included in domains of analysis and explanation.[135]

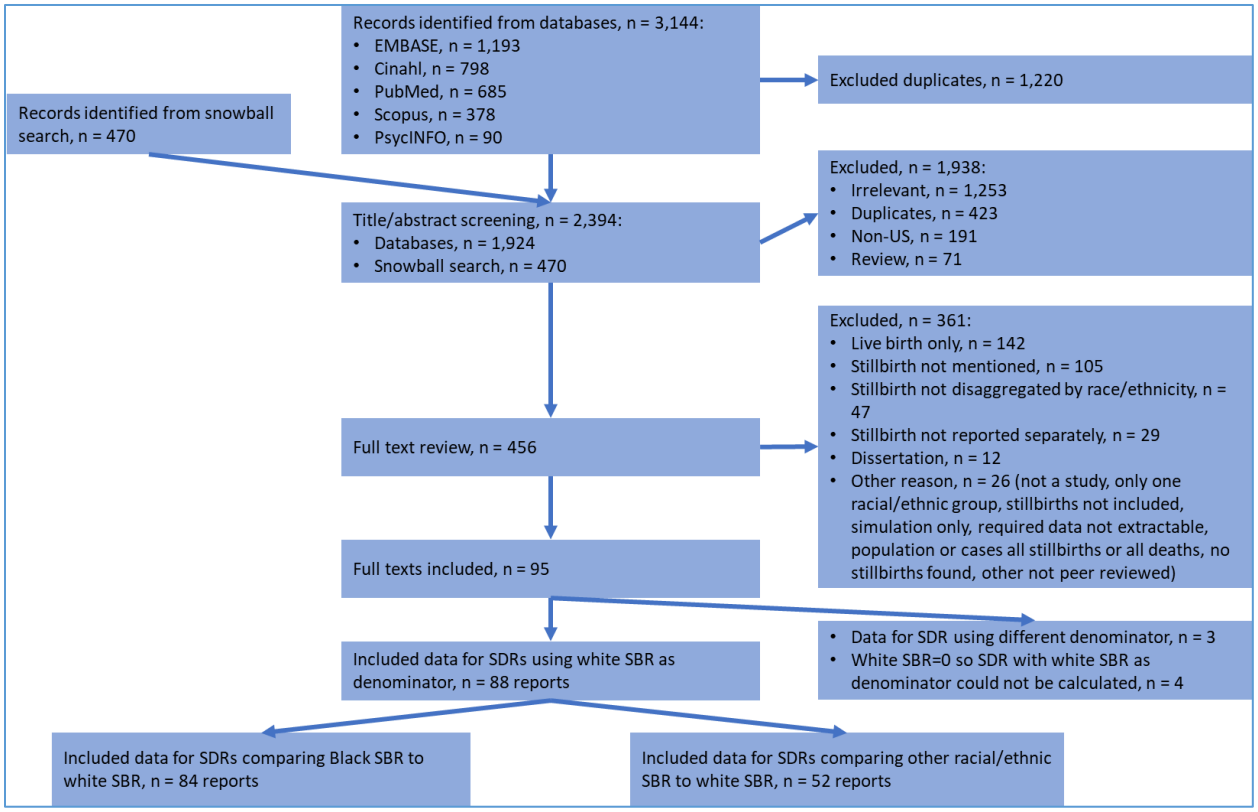

Figure 5: PRISMA flowchart showing selection of 95 included studies

Abbreviations: SBR, stillbirth rate; SDR, Stillbirth Disparity Ratio.

2.3.2 Description of included studies

There was substantial heterogeneity across the included reports. One-quarter had aims that included stillbirth, and 36% had aims that included racial disparity; 11 studies had aims that included both (12%, data not shown) (Table 1). For one-third of reports, stillbirth was the only outcome examined. Eight reports were published before 1990 (1930s, 1; 1950s, 2; 1960s, 2; 1970s, 2; 1980s, 1). Study populations had a median of 626,883 births, with nearly half being national in scope; 17% were U.S. government reports. Nearly all studies included both white and Black racial groups; less than one-quarter included Asian births. There was variation in how racial/ethnic groups were defined; Table A10 and Table A11 provide the terms used in each report. Three-quarters of reports provided a definition for stillbirth, with 18 unique definitions

used; the most common was 20 or more completed gestational weeks (38% of reports; see Table A9). Stillbirth data were limited to fetal deaths at 20 or more weeks in 58% of reports.

Table 1: Summary of characteristics of 95 included reports

Characteristic	n (%)
Study aim included stillbirth?	
Yes	23 (24%)
No, but other fetal death terms mentioned [a]	44 (46%)
No fetal death terms mentioned [b]	28 (29%)
Study aim included racial disparity?	
Yes	34 (36%)
No, but other types of racial difference mentioned [c]	46 (48%)
No racial disparity or difference mentioned	15 (16%)
Stillbirth was the only outcome studied [g]	33 (35%)
Year published	
1936-1989	8 (8%)
1990-1999	9 (9%)
2000-2009	35 (37%)
2010-2021	43 (45%)
Study population, median (range)	626,883 (102 - 71,037,685)
Racial/ethnic groups included	
White	94 (99%)
Black	90 (95%)
Hispanic	46 (48%)
Asian	21 (22%)
Native American	15 (16%)
Other [d]	20 (21%)
Location	
National	44 (46%)
Single state	25 (26%)
Multiple states	13 (14%)
Local [e]	13 (14%)
Data source	
Vital statistics	61 (64%)
Government report	*16 (17%)*
Other vital statistics	*45 (47%)*
Medical records	16 (17%)
Survey	4 (4%)
Other[f]	14 (15%)
Stillbirth definition [h]	
20+ completed weeks, no other criteria	36 (38%)
20+ with other criteria	18 (19%)
21+ completed weeks	2 (2%)
23+ completed weeks	2 (2%)
24+ completed weeks	5 (5%)
28+ completed weeks	1 (1%)
Other	8 (8%)
No definition	23 (24%)
Stillbirth data restricted to 20+ weeks?	
Yes	55 (58%)

Characteristic	n (%)
Could have also included <20 weeks	23 (24%)
Unknown [i]	17 (18%)

[a] Terms included 'fetal death', 'fetal mortality', 'spontaneous fetal death', 'fetal loss', 'preterm fetal death', 'perinatal mortality'.
[b] Terms included 'mortality', 'early mortality', 'neonatal mortality', 'pregnancy-related mortality', 'adverse birth outcomes', 'adverse perinatal outcomes', 'adverse pregnancy outcome', 'birth outcomes', 'birth rate', 'fetal conditions', 'labor induction', 'obstetric complications', 'perinatal outcomes', 'preeclampsia', 'pregnancy outcomes', 'preterm birth', 'preterm', 'severe complications of pregnancy', 'spontaneous preterm birth'.
[c] Terms included 'by race', 'differences', 'compared with', 'variation', 'association with race', 'gap', 'influence of', 'race-specific risk', 'racial trend', 'risk factor', 'contribution of', 'determinant', 'effect of race'; reports were also included in this group if the aim mentioned race only as a population subgroup.
[d] Other racial/ethnic groups included 'colored', non-Black, non-white, other, other/multiracial, other/multiracial/unknown, Black mother/white father, white mother/Black father, other non-Hispanic.
[e] Location "local" includes individual cities, counties, hospitals (below state level).
[f] "other" data source includes multiple data sources (e.g., both medical records and vital statistics).
[g] "Was stillbirth the only outcome" refers to whether the study examined only stillbirth or also other outcomes (e.g., maternal morbidity).
[h] Stillbirth definition: see Table A9 for a complete list of stillbirth definitions in the 95 included papers.
[i] Of the 72 reports with stillbirth definitions, those that only included gestational age criteria for stillbirth were by definition restricted to 20+ weeks; those that had additional criteria such as birthweight could also have included <20 week births. Of the 23 reports with no stillbirth definition, three were nonetheless restricted to 20+ weeks (results were stratified by <20.9 and 20.9+ weeks;[136] deliveries <37 weeks were excluded[137]; only births 24+ weeks were eligible[138]) and three nonetheless could have included <20 week births (ICD code for fetal death not otherwise specified included;[139] miscarriage and stillbirth grouped together as non-live birth[140]; all spontaneous terminations eligible[141]); for the remaining 17, this status was unknown.

2.3.3 Racial disparity in stillbirth rates

A total of 1,143 Black-white SDRs (Table A10) and 112 other SDRs (Table A11) were extracted:

- **Black-white:** 90 reports included Black SBRs, of which 84 had the required data to calculate Black-white SDRs; one of these reports was excluded from racial disparity reporting (see Search Results above and Appendix B).[135] The median SDR was 1.67 (Table 2). 74% of SDRs showed evidence of disparity. Median SDRs with and without 95% CIs were 1.79 (Figure 6) and 1.17 (Figure 7), respectively. The median SDR for data only including stillbirths was 1.54; the median SDR for data that may also have included fetal deaths <20 weeks was 1.87 (data not shown). There was no indication of a change in SDR magnitudes over time (Figure 8).

- **Hispanic-white:** 46 reports included Hispanic SBRs, of which 40 had the required data to calculate Hispanic-white SDRs. The median SDR was 1.09 (Figure A1). 50% of SDRs showed evidence of disparity. Median SDRs with and without 95% CIs were both 1.09.
- **Asian-white:** 21 reports included Asian SBRs, of which 18 had the required data to calculate Asian-white SDRs. The median SDR was 1.00. 39% SDRs showed evidence of disparity. Median SDRs with and without 95% CIs were both 1.00.
- **Native American-white:** 15 reports included Native American SBRs, of which 13 had the required data to calculate Native American-white SDRs. The median SDR was 1.22. 69% of SDRs showed evidence of disparity. Median SDRs with and without 95% CIs were 1.24 and 1.04, respectively.
- **Other-white:** 20 reports included other race/ethnic group SBRs, of which 18 had the required data to calculate other-white SDRs. The median SDR was 1.35. 43% of SDRs showed evidence of disparity. Median SDRs with and without 95% CIs were 1.38 and 0.92, respectively.

Table 2: Summary of Stillbirth Disparity Ratios: SDR numbers and medians stratified by whether evidence of disparity, protection, or neither; whether from adjusted estimates; and whether 95% CIs available

	Black-white			Hispanic-white			Asian-white			Native American-white			Other-white		
	# reports	# SDRs	med SDR	# reports	# SDRs	med SDR	# reports	# SDRs	med SDR	# reports	# SDRs	med SDR	# reports	# SDRs	med SDR
Total	83	1143	1.67	40	60	1.09	18	18	1.00	13	13	1.22	18	21	1.35
Evidence of…															
disparity [a]	69	847	1.89	25	30	1.22	7	7	1.30	9	9	1.26	8	9	1.95
protection [b]	22	174	0.80	9	10	0.89	6	6	0.87	2	2	0.70	2	2	0.46
neither	28	122	1.10	13	20	0.99	5	5	0.96	2	2	0.99	8	10	1.05
Constructed from adjusted estimates?															
yes	35	339	1.10	17	17	1.07	2	2	0.90	2	2	1.09	6	8	1.38
no	52	804	1.83	23	43	1.09	16	16	1.00	11	11	1.22	12	13	1.06
95% CI available?															
yes	60	814	1.79	28	45	1.09	13	13	1.00	8	8	1.24	15	18	1.38
no	32	329	1.17	12	15	1.09	5	5	1.00	5	5	1.04	3	3	0.92

Abbreviations: CI, confidence interval; med SDR, median SDR; SDR, Stillbirth Disparity Ratio.

[a] *Evidence of disparity if 95% CI available and lower bound exceeded 1, or if no 95% CI available and SDR exceeded 1.*
[b] *Evidence of protection if 95% CI available and upper bound less than 1, or if no 95% CI available and SDR less than 1.*

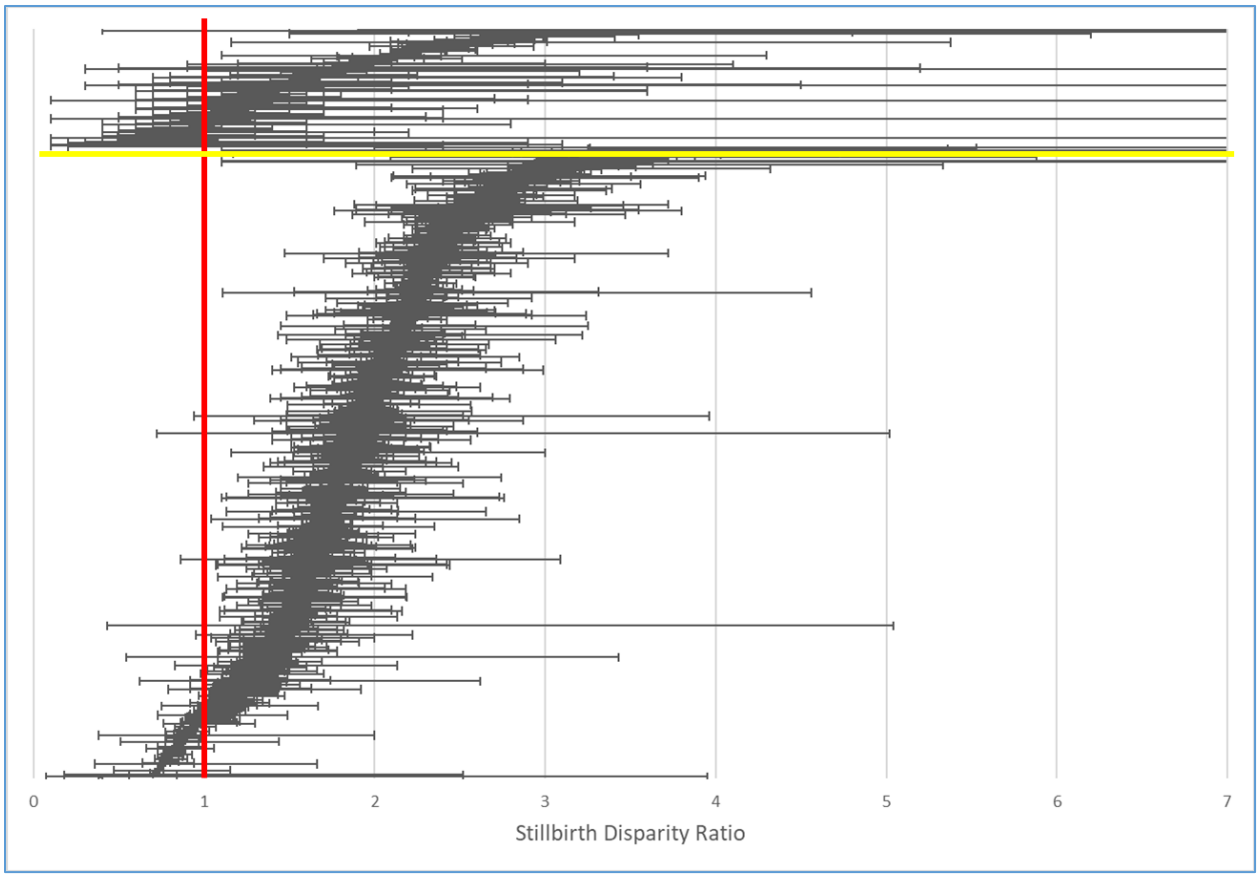

Figure 6: Black-white SDRs with 95% confidence intervals (CIs), stratified by whether adjusted (top) or unadjusted (bottom): 814 SDRs for which CIs could be computed (from 60 reports)

Abbreviations: CI, confidence interval; SDR, Stillbirth Disparity Ratio.
Yellow line separates SDRs constructed from adjusted estimates (top) from SDRs constructed from unadjusted estimates (bottom).
Red line indicates null value of 1. SDRs whose 95% CI bars are entirely to the left of the red line indicate greater risk of stillbirth in white than Black births; those with 95% CI bars entirely to the right of the red line indicate greater risk of stillbirth in Black than white births; those with 95% CI bars crossing the red line indicate no evidence of significant difference in Black and white stillbirth risk at α=5%.

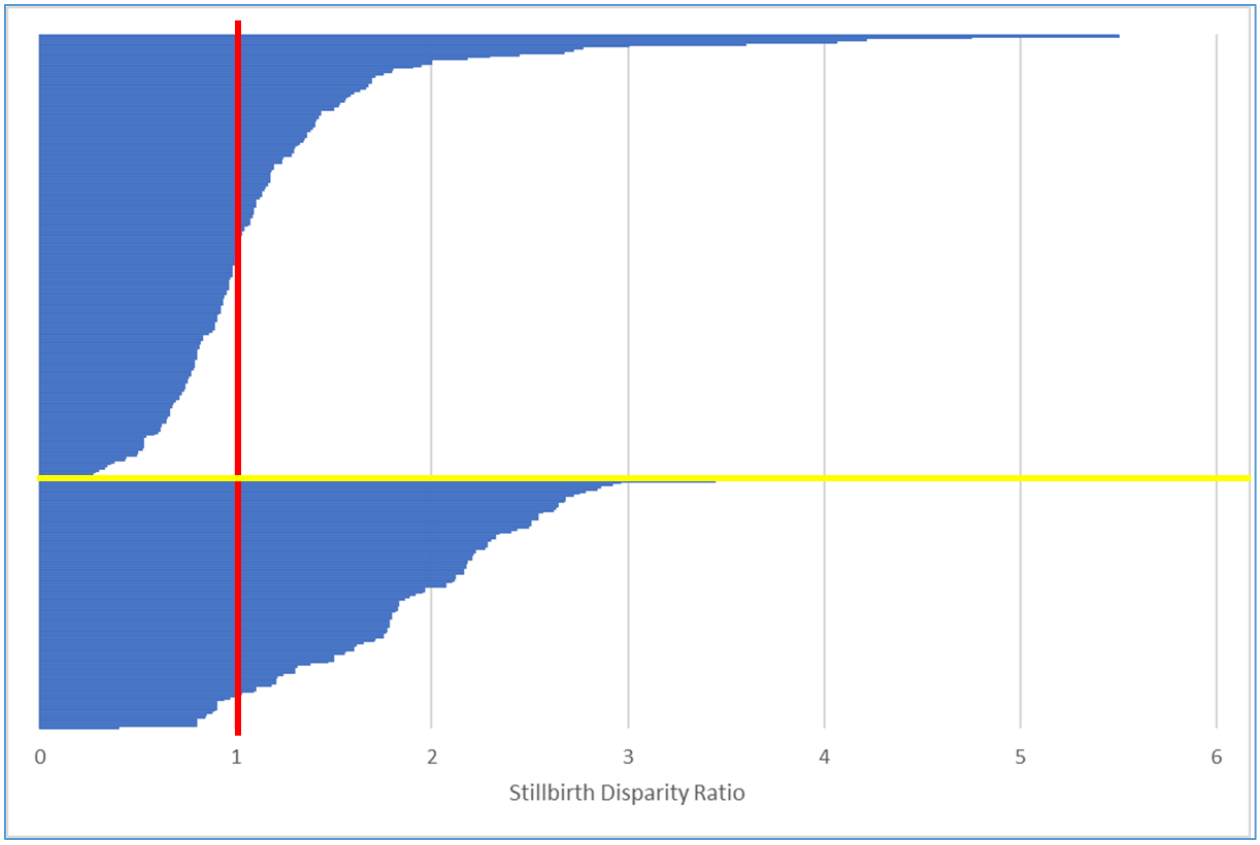

Figure 7: Black-white SDRs <u>without 95% confidence intervals (CIs),</u> stratified by whether adjusted (top) or unadjusted (bottom): 329 SDRs for which 95% CIs could not be computed (from 32 reports)

Abbreviations: CI, confidence interval; SDR, Stillbirth Disparity Ratio.
Yellow line separates SDRs constructed from adjusted estimates (top) from SDRs constructed from unadjusted estimates (bottom).
Red line indicates null value of 1. SDRs to the left of the red line indicate greater risk of stillbirth in white than Black births; those to the right of the red line indicate greater risk of stillbirth in Black than white births.

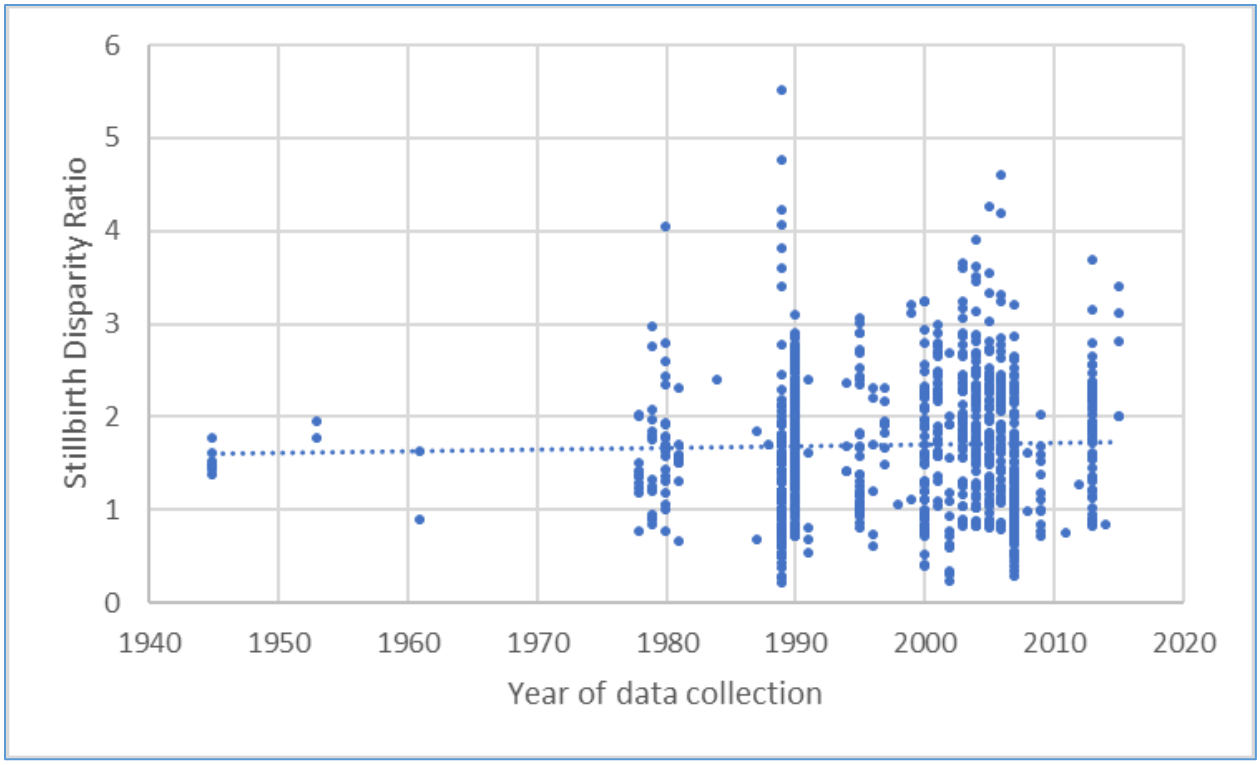

Figure 8: All Black-white SDRs, ordered by year of data collection (1945-2015), with trendline: 1141 SDRs from 82 reports

Abbreviation: SDR, Stillbirth Disparity Ratio.
Two SDRs from one report[142] not included as years of data collection were not provided. For reports with data from multiple years, only the first year of data collection was plotted.

2.3.4 Domains of analysis and explanation

Domains of analysis: 46% of the 84 reports with Black-white SDRs used fetal factors in their analytical approaches (as exposures or modifiers in regression analysis or as stratification factors in presentation of stillbirth rates), and 36% used maternal factors (see Figure 9, bottom; Table A12 for a summary; and Table A13 for details of each report). Fewer than 10% used family, community or structural factors, and none used healthcare system factors. Among fetal factors, gestational age was the most commonly used (30% of reports), followed by birth year (20%) and birthweight (12%) (see Figure 9, top). Among maternal factors, maternal age was the most common (18% of reports), followed by marital status (10%), maternal conditions,

pregnancy-related conditions, and prior adverse pregnancy outcomes (each 7%). 44% of reports conceptualized race as an exposure; by design, the remainder conceptualized race as an effect modifier or stratification factor. Five reports assessed mediation in their analytical approaches.[115 143-146]

Domains of explanation: One-third of the 84 reports made no comment on racial disparity in stillbirth rates. 56% of the reports referred to maternal factors, 42% to fetal factors, 38% to healthcare system factors, 37% to structural factors, and 20% to family or community factors. Among maternal factors, maternal conditions were mentioned in 27% of reports, maternal stress by 25%, and general (non-pregnancy-related) health by 18%. Among fetal factors, gestational age was the most commonly mentioned in relation to the observed disparity (26% of reports), followed by birthweight (8%). Among healthcare system factors, access and quality were each mentioned by 23% of reports, and among structural factors, general systemic characteristics (e.g., non-specific social and economic factors) were mentioned by 29%, and racism by 20% of reports. See Table A12 for a summary.

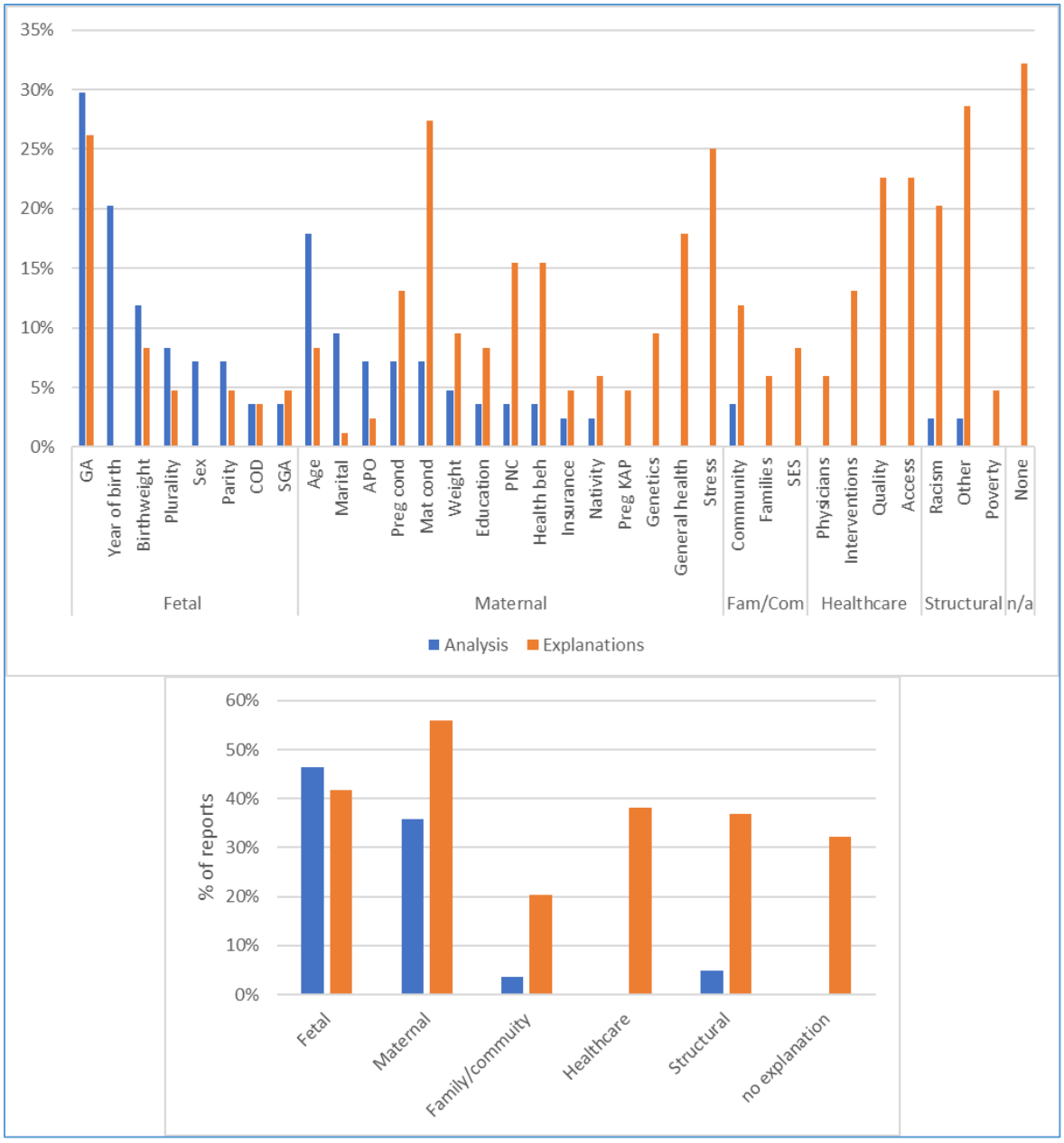

Figure 9: Domains of analysis and explanation for Black-white racial disparity in stillbirth rates (detail top, summary bottom), n=84 reports

Abbreviations: APO, adverse pregnancy outcomes; COD, cause of death; GA, gestational age; KAP, knowledge/attitudes/practice; PNC, prenatal care; SES, socioeconomic characteristics.
83 reports were included in Black-white SDR reporting but 84 reports were included in domains of analysis and explanation (see Search results above, and Appendix B).

2.3.5 Post-hoc analyses

We identified the most commonly-used categories of analysis for the 1143 Black-white SDRs: these were gestational age (used as a category of analysis for 41% of Black-white SDRs), maternal age (24%), prenatal care (14%), and education (13%) (Table 3). The majority of these SDRs showed evidence of disparity, including when we looked at SDRs within subcategories (gestational age groups, maternal age groups, trimesters of prenatal care (PNC) initiation, and educational attainment groups). Among gestational age groups, the median SDR was highest for early preterm births (1.85, Figure A2); among maternal age groups, the median SDR was highest for births to older mothers (2.15, Figure A3); among PNC groups, the median SDR was highest for mothers whose PNC started early (in trimester 1) (1.98, Figure A4); and among educational attainment groups, the median SDR was highest for mothers with a high school degree or higher (2.06, Figure A5). 33% of early preterm SDRs showed evidence of protection rather than disparity.

Table 3: Top four categories of analysis for all Black-white SDRs, for total sample and stratified by whether SDR was indicative of disparity, protection or neither

	Total			Disparity (row %) [e]		Protection (row %) [e]		Neither (row %) [e]	
	# reports [f]	# SDRs	median SDR	# reports [f]	# SDRs	# reports [f]	# SDRs	# reports [f]	# SDRs
Total	**83**	**1143**	**1.67**	**69 (83%)**	**847 (74%)**	**22 (27%)**	**174 (15%)**	**28 (34%)**	**122 (11%)**
Gestational age (all SDRs) [a]	**24**	**469**	**1.62**	**22 (92%)**	**358 (76%)**	**12 (50%)**	**96 (21%)**	**9 (38%)**	**15 (3%)**
Early PTB	18	221	1.85	14 (78%)	142 (64%)	10 (56%)	73 (33%)	5 (28%)	6 (3%)
Late PTB	11	52	1.30	11 (100%)	42 (81%)	2 (18%)	9 (17%)	1 (9%)	1 (2%)
28+ weeks	10	111	1.73	10 (100%)	106 (96%)	0	0	2 (20%)	5 (5%)
Full-term	10	49	1.57	10 (100%)	39 (80%)	1 (10%)	10 (20%)	0	0
Post-term	8	12	1.54	7 (88%)	9 (75%)	1 (13%)	1 (8%)	2 (25%)	2 (17%)
Maternal age (all SDRs) [b]	**13**	**273**	**1.89**	**12 (92%)**	**246 (90%)**	**2 (15%)**	**10 (4%)**	**4 (31%)**	**17 (6%)**
<20 years	11	80	1.61	10 (91%)	72 (90%)	2 (18%)	2 (3%)	4 (36%)	6 (8%)
20-34 years	11	105	1.98	10 (91%)	94 (90%)	2 (18%)	5 (5%)	1 (9%)	6 (6%)
35+ years	13	84	2.15	11 (85%)	76 (91%)	2 (15%)	3 (4%)	2 (15%)	5 (6%)
Prenatal care (all SDRs) [c]	**3**	**154**	**1.66**	**2 (67%)**	**135 (88%)**	**1 (33%)**	**7 (5%)**	**3 (100%)**	**12 (8%)**
Trimester 1	1	29	1.98	1 (100%)	29 (100%)	0	0	0	0
Trimester 2	1	29	1.47	1 (100%)	27 (100%)	0	0	1 (100%)	2 (7%)
Trimester 3	1	20	1.61	1 (100%)	18 (90%)	0	0	1 (100%)	2 (10%)
Any PNC	1	29	1.67	1 (100%)	29 (100%)	0	0	0	0
No PNC	2	43	1.61	2 (100%)	32 (74%)	1 (50%)	5 (12%)	2 (100%)	6 (14%)

	Total			Disparity (row %) [e]		Protection (row %) [e]		Neither (row %) [e]	
	# reports [f]	# SDRs	median SDR	# reports [f]	# SDRs	# reports [f]	# SDRs	# reports [f]	# SDRs
Education (all SDRs) [d]	**3**	**150**	**1.89**	**3 (100%)**	**139 (93%)**	**2 (67%)**	**8 (5%)**	**1 (33%)**	**3 (2%)**
Less than HS	2	58	1.73	2 (100%)	51 (88%)	1 (50%)	3 (5%)	1 (50%)	4 (7%)
HS	1	29	1.98	1 (100%)	29 (100%)	0	0	0	0
HS or more	3	20	2.06	3 (100%)	19 (95%)	0	0	1 (33%)	1 (5%)
Some college	1	39	1.98	1 (100%)	36 (92%)	0	0	1 (100%)	3 (8%)

Abbreviations: HS, high school; PTB, preterm births; SDR, Stillbirth Disparity Ratio.
[a] 24 SDRs excluded from gestational age subcategory counts (see Appendix B).
[b] 4 SDRs excluded from maternal age subcategory counts (see Appendix B).
[c] 4 SDRs excluded from prenatal care subcategory counts (see Appendix B).
[d] 4 SDRs excluded from education subcategory counts (see Appendix B).
[e] Report numbers across rows do not always sum to numbers in the Total column since a single report may have SDRs that are indicative of disparity, protection, or neither.
[f] Report numbers in columns do not always sum to totals since a single report may have SDRs in multiple subcategories (e.g. one report may have SDRs for the early PTB, late PTB, and 28+ weeks strata).

2.4 Discussion

We found 95 reports presenting stillbirth rates stratified by race/ethnicity in the U.S. We present evidence of increased risk of stillbirth in Black as compared to white births in the majority of the 83 reports with the necessary data. Among the 1143 Black-white SDRs, the median SDR was 1.67, with 74% of these SDRs showing disparity. Family and community factors, healthcare system factors, and structural factors were commonly used as domains of explanation (20-38% of reports), but rarely (family/community, structural, 4-5%) or never (healthcare system) used in analysis. The most commonly used domains of analysis—fetal and maternal factors including gestational age, maternal age, education, and prenatal care—do not appear able to explain the observed racial disparities. Gaps in the literature include a paucity of studies examining the possible role of health system, community, and structural factors in Black-white disparity in stillbirth rates, and limited data on other types of racial disparities in stillbirth rates, including Hispanic, Native American, and Asian births.

2.4.1 Interpretation of results

There is a significant literature on racial disparity in outcomes related to stillbirth. We identified three systematic or quasi-systematic reviews of racial disparity and other adverse birth outcomes, all of which yielded results consistent with our finding of racial disparity in stillbirth rates in the majority of included studies.[5 117 118] Additionally, we found several non-systematic reviews of racial disparity in birth outcomes which assessed the role of a wide range of risk factors at systemic and group as well as individual levels.[120-125] However, none commented on racial disparity in stillbirth; indeed, for most, we could not determine whether reports with stillbirth as an outcome were reviewed or excluded. The lack of clarity on whether stillbirths are included in study populations has also been found in the literature on pregnancy outcomes related to Zika infection.[147]

The present study addresses this gap in the literature by systematically updating the only extant review of racial disparity in stillbirth rates. In 2011, Hogue and Silver summarized data from 22 studies on risk factors for stillbirth that are either more common in racial/ethnic minorities or have stronger adverse associations with stillbirth in these groups. Factors identified included sociodemographic, behavioral, and pregnancy-related factors such as maternal age and education, access to prenatal care, obesity, smoking, maternal conditions such as hypertension, and spontaneous preterm birth.[1] While macro-level factors such as environmental exposures, institutionalized racism, and healthcare were mentioned, due to lack of extant research, there was no evidence to summarize for these factors. While we found four times as many relevant reports as Hogue and Silver, there were still very few which examined these macro-level factors, suggesting that there has been little change in analytical approaches to understanding racial disparity in stillbirth rates. We found just four reports that used structural factors as domains of

analysis, three of which were published after 2011.[64 81 148] This aligns with a 2016 review by Lorch et al. that focused on socioeconomic determinants of racial/ethnic disparities in preterm birth and infant mortality and briefly touched on fetal mortality, observing that the majority of the limited research on racial disparity in this outcome has focused on individual-level factors.[115]

The median Black-white SDR was 1.67, with 74% of SDRs showing evidence of disparity. Regardless of which domains of analysis were used, and which categories were used within those domains, we found that most Black-white SDRs showed evidence of greater risk of stillbirth in Black than white births, including 76% of gestational age SDRs, 88% of PNC SDRs, 90% of maternal age SDRs, and 93% of education SDRs. We also found that the majority of SDRs for all subcategories that we examined showed evidence of disparity (64-100%). Although there was some evidence that stillbirth risk in early preterm births was lower in Black than white births (33% of SDRs were protective), the median SDR for this stratum (1.85) still showed nearly twofold increased risk. These data suggest that most domains examined do not explain Black-white disparities in stillbirth rates. Interestingly, median SDRs were higher for higher educational attainment and earlier PNC start, although these are generally understood to be protective against stillbirth; however, only three reports used education or PNC as categories of analysis.

SDRs that included the null value were of interest as these indicated no Black-white disparity in stillbirth rates. There were two commonly-used categories of analysis for these SDRs: timing of stillbirth (ante- versus intrapartum; 63 SDRs, but from just one report)[149] and birthweight (24 SDRs from eight reports). Most of the SDRs using timing of stillbirth as the category of analysis were also stratified by other factors including education, maternal age and maternal conditions. It is possible that small numbers (115 Black intrapartum stillbirths in this

report) and the additional stratification by maternal conditions may account for finding no evidence of racial disparity among these SDRs. For SDRs using birthweight as the category of analysis, there was much variation across birthweight strata, with evidence of protection in low birthweight births (<1500 g, median SDR 0.88), disparity in high birthweight births (4000+ g, median SDR 3.68), and no disparity in average weight births (2000-2999 g, median SDR 1.06). At first glance, these results appear to be inconsistent with the observation that disparity is present in all gestational age strata including full-term births and the majority of preterm births. However, a distinctive feature of SDRs using birthweight as a category of analysis is that there was almost no use of other stratification factors, while most SDRs using gestational age as a stratification factor also stratified by other maternal or fetal factors; hence, it is possible that further stratification of SDRs using birthweight as the category of analysis would reveal disparities that are not apparent in these data.

The top four categories of analysis used in Black-white SDRs show a risk of stillbirth that is 60-90% higher in Black than white births regardless of which category is being examined (median SDRs 1.62-1.89 for gestational age, maternal age, PNC, and education categories), with a 30% to twofold greater risk of stillbirth in every subcategory (median SDR ranges were 1.30-1.85, 1.61-2.15, 1.47-1.98, and 1.73-2.06 for gestational age, maternal age, PNC, and education subcategories, respectively). A logical possibility is that domains of analysis which have been under- or unexamined may be at least partly responsible for the disparity.

We identified three reports which used community as a domain of analysis (in all three, the category of analysis was birthplace). Hoyert 1996 stratified national stillbirth estimates by metropolitan vs non-metropolitan counties and education.[150] All SDRs showed significant disparity, with similar median SDRs of 2.18 and 2.22 for metropolitan and non-metropolitan

counties, respectively. Cai et al. stratified stillbirth estimates by both birthplace (Kansas City vs rest of Jackson County, Missouri) and birthweight.[151] Black-white SDRs showed evidence of disparity in all birthweight strata for Kansas City but were not significant in the remainder of Jackson County (median SDRs 3.24 and 1.48, respectively). Finally, Tyler et al. stratified stillbirth estimates by U.S. region of birth and gestational age, using four regions defined by state fetal death reporting policies.[11] The median SDR for area 3 (2.07) was nearly double the median SDRs for other areas (1.25, 1.10, 1.20); however, due to lack of 95% CIs, we could not tell whether the differences are statistically significant. The authors observed that states in area 3 differed from the rest of the U.S. in having lower proportions of Black residents and lower population densities. These results suggest that disparity may vary with residential location; also, location may be a proxy for structural factors.

We found just four reports that directly used structural factors as a domain of analysis. Rammah et al. found no Black-white racial disparity in stillbirth risk with ozone exposure, though there was evidence of disparity for Hispanic births.[148] The other three reports examined measures of segregation. A historical report from 1950 stratified stillbirth risk by the proportion of non-white livebirths in residential areas, finding evidence of disparity for all SDRs, with overlapping 95% CIs and no apparent trend.[152] However, a contemporary study, Brown 2012, looked at SBRs in high segregation and low segregation counties; the respective SDRs of 2.35 (95% CI 2.16, 2.55) and 1.67 (95% CI 1.52, 1.83) had non-overlapping 95% CIs.[81] Finally, Williams 2018 examined stillbirth risk in association with changes in segregation over time.[64] Although 95% CIs for these 11 SDRs were not available, we found that three SDRs, all showing a strong protective effect (median 0.30), were constructed from Black and white SBRs with non-overlapping 95% CIs, while the remaining eight SDRs (median 0.84) were constructed from

Black and white SBRs with overlapping 95% CIs, suggesting those SDRs may not be significant. The protective SDRs compared SBRs in areas of low or decreasing segregation to areas of high segregation, while the possibly non-significant SDRs also included comparisons between areas of moderate to high segregation. This suggests that disparity varies with the degree of segregation, consistent with Brown 2012.[81]

In sum, for most of the main categories of analysis used in the 1143 Black-white SDRs, which were all maternal or fetal factors, Black-white stillbirth disparity persisted in all strata, suggesting that these individual-level factors may not fully explain the observed disparities. In the few studies that used community and structural factors of analysis, there was some evidence suggesting that area-level factors might contribute to explaining part of the disparity.

2.4.2 Strengths and limitations

This scoping review of racial disparity in stillbirth rates used comprehensive search strings with no date limits; we searched five databases and supplemented this with an extensive snowball search. While results were limited to English-language reports, our focus on the U.S. made it unlikely that relevant literature was missed for this reason. Single extraction of Black-white SDRs introduced the possibility of error, but the consistency of these data with data from the selected SDRs which were double-extracted suggested a low error rate. Moreover, we analyzed a large number of SDRs, thereby reducing the chance that errors would substantially alter our conclusions. Another limitation was our inability to calculate 95% CIs for 29% of Black-white SDRs; the median SDR was lower for SDRs without a 95% CI than with it (1.17 vs 1.79), and a larger proportion of SDRs without 95% CIs than with 95% CIs were from adjusted estimates (64% vs 16%). However, in a number of cases, the covariates adjusted for could have mediated rather than confounded associations, which would theoretically attenuate estimates of

association, at least partially explaining the difference in median SDRs. For example, parity and hypertension were adjusted for in associations between maternal age and stillbirth;[153] education in associations between maternal age and stillbirth;[149] and pregnancy complications in associations between prior C section and stillbirth;[146] all of these covariates could instead have mediated the respective associations. Further study should examine this group of SDRs more closely. It was possible that data from reports including only stillbirths (20+ weeks; 57% of reports) differed from data from reports that could have included miscarriage (<20 weeks; 43% of reports). As with research on racial disparity in stillbirth, research on racial disparity in miscarriage is sparse, but one prospective cohort study found a 57% increased hazard of miscarriage in Black vs white women, slightly lower than the median SDR we found among reports which may have included <20 week miscarriages (1.87), suggesting that factors other than gestational age at death may be responsible for the difference.[154] The small numbers of SDRs in some categories (post-term births, older maternal age), and small numbers of reports using some categories, could have biased results, while overlapping categories across reports made it difficult to assign some SDRs to subcategories. Finally, our identification of domains of analysis/explanation, and categories within each domain, was subjective, and it would be useful to validate our approach; however, the large number of SDRs extracted reduces the chances that minor changes to categories would affect our conclusions.

2.4.3 Further study

It would be of interest to extend this review to include racial/ethnic disparity in stillbirth rates outside the U.S. In particular, the reproductive, child and maternal health literature from Canada[155-161] and Australia[51 162-173] appears to be more comprehensive regarding Native populations than the U.S., and could shed light on factors to consider that might be relevant for

U.S. Native groups. A categorization of authors' comments on reasons for possibly spurious associations could also be useful in providing further context for our results. Such reasons include incompleteness of stillbirth registration[174], selective underreporting of fetal deaths[175], racial disparity in reporting and registration of stillbirths, especially early stillbirths[141 176-178], variation in fetal death reporting requirements by state[11], misclassification of fetal deaths as neonatal deaths[11], policy-related changes in fetal death reporting[179], low autopsy rates (sometimes differential by race) resulting in limited availability of data on stillbirth causes[143], differential detection of early stillbirth by race[149], and differences in reported stillbirth rates depending on methodology (traditional vs fetuses-at-risk)[11]. Quality assessment of the included reports could help to increase confidence in our results. Further research should document how race was defined and whether this is associated with data on racial disparity in stillbirth rates, as well as stratifying SDRs by whether Black and white births included Black Hispanic and white Hispanic births or not. The large number of reports included after the initial screening reflects inconsistency in stillbirth terminology: many terms are sometimes used to mean stillbirth, including apparently exclusive terms such as neonatal death[180] and infant mortality[181], so such reports needed to be included in our full text review to reduce chances of missing relevant data; it was also a consequence of the high proportion of reports that include stillbirth data but do not mention stillbirth as an outcome in abstracts.[147 182] Improved reporting of stillbirth outcomes, including better discrimination of stillbirths from neonatal deaths, would be beneficial for stillbirth research.

2.4.4 Conclusion

In 2003, Lu and Halfon carried out a non-systematic review of racial disparity in birth outcomes; while perinatal mortality was mentioned only in passing, their framework is

instructive for the study of racial disparity in stillbirth.[119] They posited that disparities in outcomes are not the result primarily of disparities in characteristics experienced and measured in pregnancy such as prenatal care, health behaviors, infection, and socioeconomic status, although these are among the factors most commonly examined and implicated. Instead, disparities in birth outcomes are the product of differential exposure and response to both risk and protective factors over the life-course, via both early life adversity (the developmental origins of disease model) and cumulative stress (the weathering model), with differences sometimes persisting intergenerationally. Such a model calls for an integrated approach to lifecourse research at all levels from the individual to the structural.

Two non-systematic global reviews of stillbirth in high-income countries by Flenady et al. in 2011 and 2016 subsequently underlined the importance of structural as well as individual-level explanations for disparities in stillbirth rates between racial/ethnic groups, including socioeconomic deprivation and racism.[8 183] And the few (non-systematic) reviews which have included stillbirth have also acknowledged the role of community and policy-level factors. For instance, a review by Ranjit et al. on racial disparity in low birthweight, intrauterine growth restriction (IUGR), and fetal and infant mortality in relation to bisphenol A (BPA), an endocrine disrupting chemical found in some plastics, observed that racial disparity in exposure to BPA was itself due partly to group-level factors such as segregation and neighborhood poverty, and as such, interventions at the individual level are unlikely to sustainably reduce the observed racial disparity.[114] Other reviews have reached similar conclusions.[116]

The present study demonstrates that in the intervening 20 years since Lu and Halfon argued for a multilevel, integrated, life-course approach to understanding racial disparity in infant and perinatal mortality, little has changed for research on stillbirth. Data conclusively

point to a persistently greater risk of stillbirth for Black as compared to white families regardless of the analytical approach that is taken. The answers to this puzzle may reside in the domains that remain under-investigated: community, healthcare system, and structural domains. Factors which have so far circumscribed the literature on racial disparity in stillbirth should be identified so that they can be overcome. Researcher or funder bias may partially account for the continued emphasis on individual (fetal and maternal) factors to the exclusion of group factors which can only be addressed at a policy or all-of-society level.

Chapter 3: Can structural racism help to explain Black-white disparity in stillbirth rates?

3.1 Introduction

The stillbirth rate (SBR) is an indicator of inequity in public health.[7] The U.S. SBR is 5.7 per 1000 total births, but in non-Hispanic (NH) white families it is 4.7, while in NH Black families, it is 10.4.[1 2 20 109] Despite a century of persistently doubled SBRs in Black families, the literature remains sparse, inconclusive, and focused on proximate factors that leave this disparity unexplained.[1] For instance, studies have found racial disparity in SBRs regardless of prenatal care, education, age, smoking, hypertension, diabetes, and obesity.[4 149 184-187] The inability of existing research to explain the disparity provides a rationale to look to distal factors for explanations.[1 2 115 177 185 186 188 189]

Structural racism is an interdependent, self-perpetuating complex of institutional practices, laws, and policies that oppresses members of a racial/ethnic group *because of* their group membership; it has been described as a fundamental cause of health inequities.[63 190-193] Since structural racism targets racial/ethnic minority individuals due to their group membership, and does not target white individuals, it necessarily affects racial/ethnic minority individuals and white individuals differently.[194] As a macro-level feature, structural racism is distinct from individual-level racism.[193] It has been associated with multiple adverse health outcomes,[64 190 195-202] with associations often varying by race/ethnicity.[200 203] Structural racism may be associated with stillbirth through multiple pathways, influencing access to and quality of healthcare, determining the types of healthcare available, or the degree of healthcare practitioner bias, ultimately affecting maternal and fetal medical conditions. It may influence environmental

factors such as pollution or neighborhood quality (e.g., availability of affordable foods, employment opportunities, housing and transportation), with follow-on effects on household income affecting insurance, maternal conditions, or access to care; or it may increase maternal psychosocial stress, either directly, or through exposure to individual-level racism or discrimination, affecting maternal stress responses, increasing vulnerability to infection and threatening fetal survival.[63 190 204 205] Most likely, these pathways are intertwined and make simultaneous contributions to risk. According to the theory of Fundamental Causes, structural causes by their very nature continually create replacement mechanisms at intermediate and individual levels that perpetuate health inequities. This is the reason that non-structural interventions can never sustainably remove health inequities.[62]

Due to its multidimensional nature (with impacts manifesting, for example, in the housing, employment, education, and healthcare sectors as well as the justice system)[190 191], structural racism cannot be fully captured by a single measure, hence best practice is to use multiple measures.[190 193 206] Segregation, which geographically isolates racial/ethnic groups, often in areas of low resource and opportunity, is one of the most commonly-examined measures of structural racism.[152 193 199 206-210] The U.S. government acknowledges segregation as a social determinant of racial inequities in health outcomes.[211] As with structural racism itself, segregation has multiple dimensions (Table A41) and measures (Table A42). The five domains originally described by Massey and Denton in 1988[212] include isolation (the probability that minority and majority groups will come into contact), evenness (how closely racial distributions within neighborhoods mirror the racial distribution of the larger region), clustering (the degree to which minority neighborhoods are close together), centralization (the degree to which a racial/ethnic group is located within the central region of a given area), and concentration (the

degree to which a minority population is concentrated within a region).[212-214] The most commonly used measures are the Indices of Dissimilarity and Isolation.[212-214] These measures have, however, been criticized for inadequately accounting for segregation's spatial nature.[215] The Index of Concentration at the Extremes (ICE) was developed to address this and other limitations of more traditional measures. ICE quantifies the degree to which neighborhoods are composed of "privileged" or "disadvantaged" individuals.[216-218] By defining privilege and disadvantage using multiple characteristics, ICE can model not only residential segregation, but also what has been termed racialized economic segregation.[216 218] ICE is most commonly represented by race, income, or a combination of the two (see Appendix B). The use of ICE has been increasingly used in research on segregation and health outcomes, including all-cause mortality[219], cancer[220], assault[221], infant mortality[218], preterm birth,[222] and neonatal morbidity and mortality.[223]

The burden of stillbirth is inequitably borne by Black mothers in the U.S. Reasons for the persistent racial disparity are unknown, but structural racism presents a plausible macro-level explanation.[189] Notably, however, there has been little research on structural factors. Only two studies have sought to evaluate the role of structural racism in relation to stillbirth; each examined only one dimension of structural racism.[64 81] Brown et al. found that residence in counties with high vs low segregation was associated with increased odds of stillbirth only in NH Black but not NH white births,[81] and Williams et al. found that reduced segregation as measured by the Indices of Dissimilarity and Isolation was often associated with lower odds of stillbirth in Black births but had no association with stillbirth in white births; however, in some cases there was a stronger protective effect of reduced segregation in white than Black births.[64]

We assessed whether structural racism helps to explain Black-white disparity in stillbirth

rates in ten years of births in NYC. Recognizing that structural racism, not race, is an upstream cause of disparities, we conceptualized structural racism, not race, as the exposure of interest.[224-226] Results that would be consistent with our hypothesis that structural racism is an upstream cause of racial disparity in stillbirth rates included positive associations between structural racism and stillbirth in Black but not white births, or stronger positive associations in Black than white births.

3.2 Methods

3.2.1 Study population and data sources

The study population included all 1,077,041 livebirths and stillbirths registered with NYC's Department of Health and Mental Hygiene (DOHMH) between 2009 and 2018, other than births to non-residents, births at <20 completed gestational weeks, and multiples. NYC was selected because of its high stillbirth numbers and rates and its relatively high level of racial segregation in comparison to other U.S. cities. Individual-level data (outcome and covariates) were from DOHMH's Vital Statistics and Spontaneous Terminations of Pregnancy Registries. Group-level data (exposures and covariates) were from U.S. Census American Community Survey (ACS) datasets for 2009-2013 (referred to as "vintage 2013") and 2014-2018 ("vintage 2018").

3.2.2 Exposures

Structural racism was measured at the level of the PUMA (Public Use Microdata Area). NYC has 55 PUMAs, each with a population of at least 100,000. Births were assigned exposure values based on birth year and PUMA of mother's residence (Table A15 and Appendix B).

Structural racism was represented by four exposures. The Indices of Dissimilarity and Isolation (Dissimilarity and Isolation) measure the segregation domains of unevenness and isolation, respectively, and are the only measures of structural racism that have been used in studies of stillbirth.[64 81 212] We constructed them from race/ethnicity data aggregated from NYC's 2,168 census tracts. For ICE, we followed the literature and defined "privilege" and "disadvantage" as NH white households earning $100,000+ and Black households earning <$25,000 annually, respectively.[218 221 223] We chose a combination of race and income to complement the traditional Indices of Dissimilarity and Isolation which are purely race-based, in order to introduce an additional dimension of structural racism, namely economic inequity. ICE represents the difference between numbers of "privileged" and "disadvantaged" households as a proportion of the total population in a given neighborhood (see Table A14 for the formula). As such, it is a relative, not absolute, measure. Hence, the relationship between ICE and absolute measures of racial composition and poverty can be thought of as similar to the relationship between a country's Gini coefficient (a measure of inequity, or relative wealth) and its poverty level (a measure of absolute wealth), where the absolute measures reflect the total population but the relative measures quantify extremes. Just as countries' Gini coefficients and poverty rates may differ substantially, so too may a neighborhood's ICE, poverty, and racial composition measures. See Appendix B for a more complete discussion of this measure. The **Educational Inequity Ratio** (Educational Inequity) quantifies the relative educational attainment of Black vs NH white adults.[197 200 201] Note that ICE used household data while the other exposures used individual data; throughout, we use "residents" to refer to both households and individuals.

3.2.3 Analytic approach

Descriptive analysis: We carried out descriptive analyses, presenting *p*-values for comparisons within race groups and comparing births with and without PUMA data. Missingness was retained as a separate category for all covariates as it was not at random.

Primary analysis: After excluding births lacking PUMA data (n=334), we tested for interaction between race (NH Black or NH white) and structural racism exposures in relation to stillbirth. For exposures showing statistically significant interactions with race ($p<0.05$ for cross-product terms; for tertile 3 or quintile 5 for categorical versions of exposures), all subsequent analyses were performed separately in NH Black (n=221,925) and NH white (n=325,058) births.

We used multilevel logistic regression with random intercepts to estimate associations between structural racism and stillbirth, exponentiating regression coefficients to obtain odds ratios and their 95% confidence intervals (CIs). We used categorical versions of the exposures for the primary analyses, based on the literature which gives evidence of dose-response relationships between these structural racism measures and perinatal outcomes (e.g., [64 202]). We also report results from models using continuous versions of the exposures in Appendix A. In further studies, we will use results from our primary analyses to inform development of these models (using the continuous versions of the exposures).

Main models adjusted for the following five covariates:

- **Individual level:**
    - **Year of birth** (continuous), because it is associated with stillbirth (the SBR has gradually declined) and could affect exposures (e.g., a gradual decline in segregation over time).[64 227]
    - **Maternal age** (continuous, with a quadratic term to model the U-shaped

association with stillbirth). Maternal age is a risk factor for stillbirth; it could also be associated with structural racism measures through affecting peoples' choices of where to live and their ability to act on those choices, in part through also affecting their educational attainment and individual or household income. Below, we explain a secondary analysis that treated maternal age as an effect modifier rather than confounder.

- **Maternal education** (a four-category covariate since a continuous version was unavailable). Education is another risk factor for stillbirth, and could also affect the segregation indices (Dissimilarity and Isolation) and ICE through affecting the choices people make about where they live, and through an income pathway, also affecting their ability to take action on those choices. Individual education necessarily also affects Educational Inequity, as this exposure is constructed from the educational attainment of individuals, sorted into racial groups. However, individual education may also be affected by structural racism, potentially making it a mediator rather than confounder.[228] For instance, segregation may affect the availability of and access to educational resources such as community colleges, and the presence of educational inequity in a neighborhood may affect social pressure and support for continuing education. Finally, education both contributes to, and may be affected by, PUMA-level poverty and educational attainment. Our aim was to provide an unbiased estimate of the total effect of structural racism on stillbirth, meaning its effect through all pathways. Therefore, we adjusted for education in our main analyses (assuming it is a confounder, but risking a possible underestimate if it is a mediator) and excluded it in sensitivity analyses (assuming

it is a mediator, and risking a possible overestimate if it is a confounder).

- **PUMA level:**
    - **PUMA proportion NH Black (PUMA % Black)**: The proportion of the PUMA population consisting of Black residents was likely a confounder. It may affect stillbirth through affecting the quality of available prenatal care (PNC) or indirectly through affecting employment opportunities that affect stillbirth through income and insurance pathways. It may also affect ICE, segregation and educational inequity measures, e.g., through income pathways. Importantly, adjusting for this covariate was also necessary in order to control for baseline levels of Black populations in each PUMA.[197] ICE in particular is a relative, not absolute, measure of both race and poverty, and the numerator does not include data on non-poor Black or non-wealthy white individuals. Adjusting for the absolute level of Black populations is akin to adjusting for baseline levels of blood lead in studies of child blood lead exposure, ensuring that estimates of association between structural racism and stillbirth are not confounded by PUMA % Black "starting points".[203 229] Much of the literature on exposures such as Isolation and Dissimilarity takes a similar approach.[197 200 209 213 230-232] Also, adjusting for this covariate could help to address small numbers of Black individuals in some areas, which can lead to random variation in segregation index values; this is why the U.S. Census study of segregation weighted the Dissimilarity and Isolation Indices by the proportion of the population composed of Black individuals.[227] To assess whether adjusting for this covariate introduced over-adjustment bias, in a sensitivity analysis, we excluded it.

- **PUMA % poverty**: The percent of PUMA households living under the NYC poverty line (using the NYC Center for Economic Opportunity threshold)[233 234] was also likely a confounder. Neighborhood-level poverty may affect stillbirth by affecting the availability and quality of PNC and healthcare generally, maternal medical conditions and environmental risk factors, as well as through affecting employment opportunities and thereby household income. Neighborhood-level poverty may also influence structural racism measures, including Educational Inequity (e.g., through affecting educational opportunities such as school availability) and segregation (e.g., through affecting the availability of affordable housing and the variety of employment opportunities, thereby influencing people's choices of where to live). In particular, we needed to adjust for PUMA % Poverty in models with ICE as the exposure in order to control for baseline levels of one component of ICE, income inequality. The rationale was the same as that for adjusting for PUMA % Black—to ensure baseline levels of poverty are not confounding estimates of association. As with PUMA % Black, much of the relevant literature takes a similar approach.[64 197 199 200 203 230 232 235-237] To assess whether adjusting for this covariate introduced over-adjustment bias, in a sensitivity analysis, we excluded it.

Our interest was to estimate the total effect of structural racism on stillbirth; therefore, we did not adjust for individual-level covariates such as maternal medical conditions, PNC visits, and insurance status that we hypothesized could act *only* as mediators of these associations. See Appendix B for more information, and Figure A6 for the theoretical diagram. We used Z-scores for all continuous covariates to improve interpretability and assist with model convergence.

We carried out the following sensitivity analyses:

- **Sensitivity analysis 1**: Investigated different model specifications: (a) excluded maternal education from the model because education might mediate rather than confound associations; (b) excluded PUMA % poverty and PUMA % Black to assess whether there was evidence of overadjustment; and (c) additionally adjusted for a sixth covariate, **PUMA educational attainment** (PUMA % HS). This may affect stillbirth through affecting the quality of PNC in the PUMA as well as through income and employment pathways, and indirectly through affecting individual educational attainment. Additionally, it may both affect and be affected by both PUMA-level poverty and structural racism measures, through affecting the choices people make and actions that they take regarding where to live. Similar studies have also adjusted for this covariate.[81 209 232] This covariate was strongly correlated with PUMA % poverty, however; hence we excluded it from main models to avoid collinearity, but an analysis of the theoretical diagram for our hypothesized associations indicated that it was in the minimum sufficient adjustment set;
- **Sensitivity analysis 2**: Used alternative versions of the exposures (Table A14);
- **Sensitivity analysis 3**: Used extreme versions of the exposures, created by dichotomizing the continuous versions at the 75th percentile of the PUMA distribution to check that we had not missed associations with extreme values;[201]
- **Sensitivity analysis 4**: Excluded births in PUMAs with <5 and <10 stillbirths[238] and stillbirths with reported birthweight <150 grams;
- **Sensitivity analysis 5**: Stratified by period (2009-2013 and 2014-2018), corresponding to the two ACS vintages;

- **Sensitivity analysis 6**: Assessed potential bias due to sibling clusters by running regression in two years chosen at random from each vintage (2009, 2016), based on the assumption that there would be few siblings in single years. In post-hoc analyses, we selected two different years (2011, 2018) due to variation in stillbirth data before and after 2011, when NYC began implementing the national Standard Report of Fetal Death.[239]

Secondary analysis: The "weathering hypothesis" predicts that stress accumulates over the lifecourse in Black women due to social inequities and disparity, such that age is a relatively greater risk factor for a wide range of adverse health outcomes in Black than white women.[153 205] Premature ageing may also increase susceptibility to stressors such as structural racism. The weathering hypothesis would thus predict that Black-white disparity in stillbirth rates will be greater in older than younger mothers. We therefore carried out exploratory analyses to estimate race-specific ORs for structural racism and stillbirth stratified by age group. We relaxed the requirement of evidence for interaction to $p<0.1$ for the X^2 test comparing models with and without interaction terms, due to smaller stillbirth numbers per PUMA in race- and age-defined strata. In a sensitivity analysis, we further adjusted for PUMA % HS to align with the minimum sufficient adjustment set from our theoretical diagram.

3.2.4 Ethics

This study was determined to be exempt by the Columbia University Human Research Protection Office Institutional Review Board.

3.2.5 Software

All analysis used R.

3.3 Results

3.3.1 Descriptive epidemiology of stillbirths in NYC 2009-2018

There were 8,177 stillbirths and 1,068,864 livebirths in NYC in 2009-2018, with an SBR of 7.6 per 1000 total births. There was much variation in SBRs across race (Table 4). The SBR was 13.8 in NH Black families and 4.7 in NH white families. The SBR was significantly higher in males than females for NH Black but not NH white births. The very preterm SBR in NH Black births was lower than the very preterm SBR in NH white births, while the full-term SBR in NH Black births was nearly double that in NH white births. In NH white families, the SBR was highest among teenaged mothers; in NH Black families, it was highest among older mothers. The SBR was twice as high in NH Black as NH white mothers with a high school diploma or less, and nearly three times as high in NH Black as NH white mothers with at least some college.

SBRs varied by borough and race, and across PUMAs, but there was little variation in structural racism measures across vintages (Figure A7, Table A15, Table A16). The Bronx and Manhattan had the highest and lowest SBRs for NH white families, respectively, but for NH Black families, the boroughs with the highest and lowest SBRs were Staten Island and Queens, respectively. For NH white families, the SBR was highest in PUMAs in ICE quintile 1 (concentration of disadvantage), in Isolation tertile 3 (most isolated), and with % Black above the median. For NH Black families, these patterns were reversed (Figure 10). In NH white families, SBRs were higher in PUMAs with % poverty above vs below the median, while in NH Black families, SBRs were similar regardless of PUMA % poverty. Numbers of stillbirths and livebirths stratified by PUMA-level covariates and race are in Table A17. PUMA was missing for 334 births, of which 95% were stillbirths (Table A18). Stillbirths missing PUMA data were

more likely to be very preterm than stillbirths with PUMA data, and to have been born in the first five years of the study period.

Table 4: Maternal, birth, and PUMA-level characteristics for NYC births 2009-2018, including stillbirth rates and numbers of births for total sample and stratified by race

	Total			Non-Hispanic Black			Non-Hispanic white		
	Livebirths + stillbirths	SBR	*P* value [e]	Livebirths + stillbirths	SBR	*P* value [f]	Livebirths + stillbirths	SBR	*P* value [f]
Total	1,077,041	7.6		222,047	13.8		325,113	4.7	
Birth characteristics									
Sex			<0.01*			<0.01*			<0.46
Female	524,209	6.0		108,832	10.4		157,202	3.7	
Male	551,458	6.7		112,743	12.9		167,590	3.6	
Missing	1,374	1000		472	1000		321	1000	
Gestational age			<0.01*			<0.01*			<0.01*
20-27 w	10,306	483.5		4,451	452.5		1,422	571.0	
28-36 w	73,682	26.5		21,657	32.6		15,042	25.3	
37-47 w	993,053	1.3		195,939	1.8		308,649	1.0	
Year of birth			<0.01*			<0.21			<0.26
2009	113,450	8.3		25,513	15.0		31,279	5.4	
2010	111,506	8.0		24,795	14.4		30,958	4.8	
2011	110,232	8.3		24,082	15.8		31,755	4.7	
2012	110,233	7.5		23,044	12.9		32,204	5.1	
2013	107,283	7.2		22,159	12.6		32,602	4.1	
2014	108,389	7.8		21,795	13.0		33,239	4.6	
2015	107,709	7.0		21,211	13.1		33,462	4.2	
2016	105,944	7.2		20,428	14.3		33,397	4.2	
2017	102,565	7.1		19,918	13.5		33,111	4.6	
2018	99,730	7.4		19,102	12.7		33,106	5.0	
Maternal characteristics									
Maternal age			<0.01*			<0.01*			<0.01*
10-19 y	48,766	9.6		14,401	14.4		3,845	5.7	
20-34 y	783,945	7.0		160,831	12.8		226,274	4.3	
35-63 y	244,325	9.0		46,815	17.2		94,993	5.4	
Missing	5	1000		-			1	1000	
Borough			<0.01*			<0.01*			<0.01*
Bronx	195,940	9.5		57,722	13.1		11,266	7.5	
Brooklyn	395,511	8.3		96,704	15.1		161,677	5.3	
Manhattan	175,273	5.5		20,866	12.3		77,306	3.3	
Queens	258,747	6.6		40,152	11.8		47,880	4.1	
Staten Island	51,570	6.9		6,603	16.8		26,984	4.7	
Education			<0.01*			<0.01*			<0.01*
HS or less	479,651	5.3		105,372	9.4		90,639	4.6	
Any college	436,135	2.8		100,026	5.2		139,769	1.8	
> college	153,660	1.8		13,964	3.9		93,331	1.4	
Missing	7,595	543.0		2,685	556.1		1,374	516.0	
Race/ethnicity			<0.01*						
NH Black	222,047	13.8							
NH white	325,113	4.7							
Hispanic	336,060	6.2							
NH Asian	176,403	4.4							
NH Native	517	7.7							
Other	13,246	4.2							

	Total			Non-Hispanic Black			Non-Hispanic white		
	Livebirths + stillbirths	SBR	*P* value [e]	Livebirths + stillbirths	SBR	*P* value [f]	Livebirths + stillbirths	SBR	*P* value [f]
Missing	3,655	182.8							
Medical factors			<0.01*			<0.01*			<0.01*
Yes	541,092	6.9		140,129	11.7		129,332	4.0	
No	535,911	8.2		81,899	17.2		195,773	5.1	
Missing	38	1000		19	1000		8	1000	
# PNC visits			<0.01*			<0.01*			<0.01*
<median	489,205	13.1		117,369	20.9		133,982	8.5	
median+	587,836	3.0		104,678	5.8		191,131	2.0	
Structural racism measures [d]									
ICE [h]			<0.01*			<0.01*			<0.01*
Quintile 1	231,298	10.8		108,321	13.8		17,552	6.8	
Quintile 2	206,584	8.5		68,707	12.1		22,914	5.6	
Quintile 3	208,062	6.8		28,476	12.9		45,093	4.6	
Quintile 4	237,901	5.5		8,810	14.6		112,307	4.8	
Quintile 5	192,862	4.7		7,611	16.7		127,192	3.6	
Isolation [g]			<0.01*			<0.01*			<0.01*
Tertile 1	399,064	5.2		10,577	17.7		215,151	4.3	
Tertile 2	313,655	6.4		45,185	12.0		71,814	4.1	
Tertile 3	363,988	10.4		166,163	13.3		38,093	6.2	
Dissimilarity [g]			<0.01*			<0.24			<0.01*
Tertile 1	358,990	7.3		79,738	12.7		95,924	4.2	
Tertile 2	333,041	6.6		50,164	13.8		116,218	4.1	
Tertile 3	384,676	7.9		92,023	13.5		112,916	5.1	
Ed Inequity [g]			<0.01			<0.09			<0.16
Tertile 1	361,274	7.2		76,124	12.5		103,186	4.7	
Tertile 2	362,580	7.7		77,650	13.6		92,705	4.2	
Tertile 3	352,853	7.0		68,151	13.7		129,167	4.5	
Other PUMA characteristics [d]									
PUMA % poverty [a]			<0.01*			<0.80			<0.01*
<median	469,704	6.3		75,644	13.2		196,790	3.9	
median+	607,003	8.0		146,281	13.3		128,268	5.4	
PUMA % Black [b]			<0.01*			<0.18			<0.01*
<median	565,351	5.2		22,210	14.3		253,332	4.2	
median+	511,356	9.6		199,715	13.2		71,726	5.5	
PUMA % HS [c]			<0.01*			<0.28			<0.01*
<median	604,020	7.7		128,392	13.0		103,846	5.3	
median+	472,687	6.7		93,533	13.6		221,212	4.1	

Abbreviations: HS, high school; ICE, Index of Concentration at the Extremes; NH, non-Hispanic; PNC, prenatal care; PUMA, Public Use Microdata Area; SBR, stillbirth rate (number of stillbirths per 1000 total births); w, weeks; y, years.

[a] PUMA % Poverty, proportion of the PUMA population below the NYC poverty line

[b] PUMA % Black, proportion of the PUMA population consisting of NH Black residents

[c] PUMA % HS, proportion of the PUMA population with at least a high school diploma

[d] PUMA not available for 334 births, of which 318 were stillbirths (122 NH Black births of which 117 stillbirths, and 55 NH white births of which 51 stillbirths)

*[e] P values are from X^2 tests of association between stillbirth/livebirth status and the respective categorical covariate in the total population. Bonferroni correction for 15 comparisons produces 0.05/15 ~ 0.0033 as the 5% α significance level; P values <0.0033 are followed by *.*

*[f] P values are from X^2 tests of association between stillbirth/livebirth status and the respective categorical covariate in NH Black or NH white births. Bonferroni correction for 15 comparisons produces 0.05/15 ~ 0.0033 as the 5% α significance level; P values <0.0033 are followed by *.*

[g] *Tertile 1 indicates least isolated, segregated or inequitable; tertile 3 indicates most isolated, segregated, or inequitable.*
[h] *Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.*

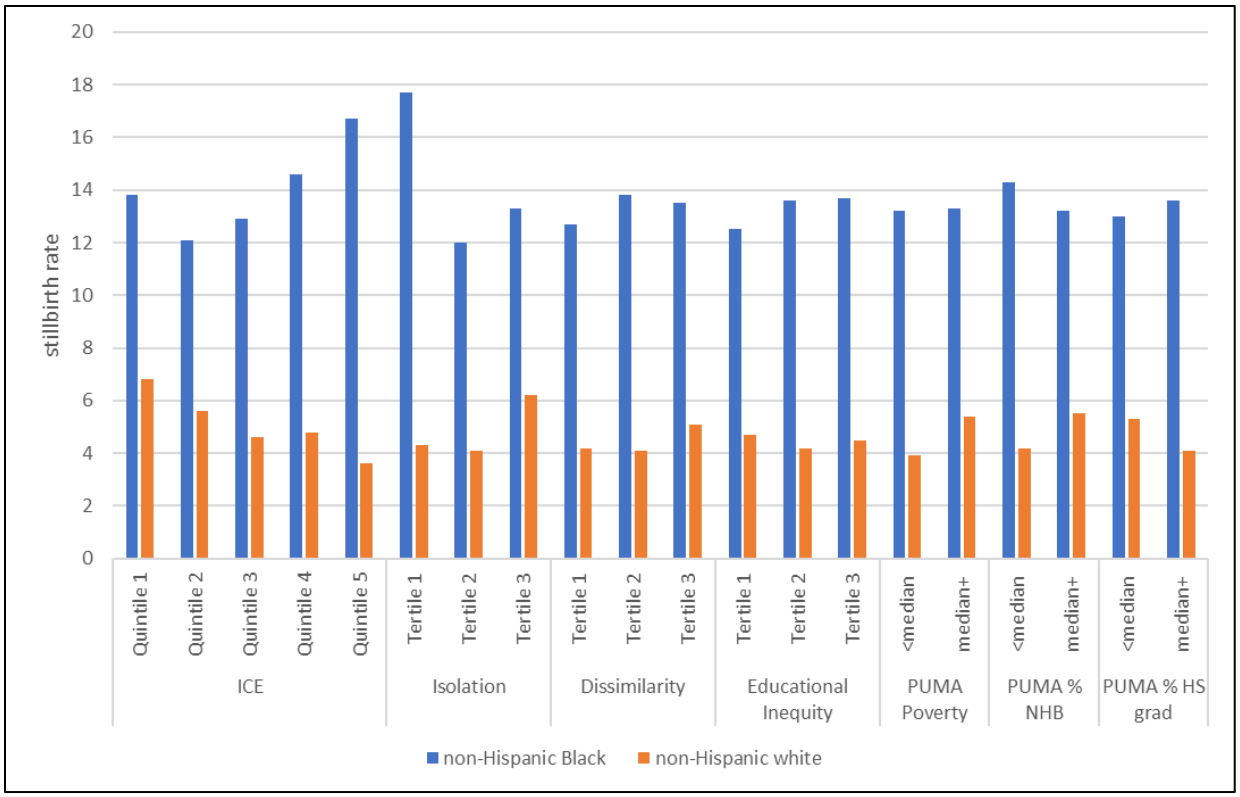

Figure 10: Stillbirth rates (number of stillbirths per 1000 total births) for four measures of structural racism and in PUMAs above and below the median for PUMA-level characteristics, stratified by race, 2009-2018

Abbreviations: HS grad, high school graduate; ICE, Index of Concentration at the Extremes; NHB, non-Hispanic Black; PUMA, Public Use Microdata Area.

3.3.2 Associations between structural racism and stillbirth

ICE and Isolation were negatively correlated (r = -0.86), as were PUMA % poverty and PUMA % HS (r = -0.83) (Table A19). There was also strong correlation between Isolation and PUMA % Black, and between ICE and both PUMA % Black and PUMA % poverty. Correlation was low between PUMA % Black and PUMA % poverty. Dissimilarity and ICE were associated with stillbirth in the combined population of NH Black and white births in models that adjusted

for race, with ORs of 1.16 (Dissimilarity tertile 3 vs 1, 95% CI 1.03, 1.31) and 1.44 (ICE quintile 5 vs 1, 95% CI 1.01, 2.06), respectively (Table A20). There was no evidence of associations between Educational Inequity or Isolation and stillbirth in the combined population. We found that associations between stillbirth and both Isolation and ICE varied significantly with race (p<0.05 for the relevant cross-product terms); there was no evidence of interaction for Educational Inequity or Dissimilarity. Hence, subsequent analyses were performed only for Isolation and ICE.

Among NH Black mothers, living in a PUMA with a high concentration of privilege vs disadvantage was associated with 70% to 90% increased odds of stillbirth (ICE quintile 5 vs 1 OR 1.90, 95% CI 1.20, 2.99; Table 5). Living in a PUMA with high vs low Isolation was associated with 39% to 40% lower odds of stillbirth (Tertile 3 vs 1 OR 0.60, 95% CI 0.42, 0.86). Tests for trend were significant for both structural racism measures. Among NH white mothers, there was no evidence for associations between either ICE or Isolation and stillbirth. Models using continuous versions of the exposures produced weaker estimates of association, albeit in the same direction (Table A21), and models using an alternative version of Isolation no longer showed evidence of an association with stillbirth in NH Black mothers (Table A26); other sensitivity analyses were largely consistent with results from the primary analyses (Table A22-Table A30).

Table 5: Odds ratios (95% CI) for associations between two structural racism measures (Isolation and ICE) and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]			
	NH Black (n=221,925)	*P* value [d]	NH white (n=325,058)	*P* value [d]
Isolation [b]		<0.01		<0.49
Tertile 1	ref		ref	
Tertile 2	0.61 (0.47, 0.80)		1.04 (0.81, 1.35)	
Tertile 3	0.60 (0.42, 0.86)		1.28 (0.77, 2.14)	

	OR (95% CI) [a]			
	NH Black (n=221,925)	*P* value [d]	NH white (n=325,058)	*P* value [d]
ICE [c]		<0.01		<0.35
Quintile 1	ref		ref	
Quintile 2	1.12 (0.95, 1.33)		0.99 (0.68, 1.45)	
Quintile 3	1.27 (0.95, 1.70)		1.10 (0.66, 1.85)	
Quintile 4	1.70 (1.16, 2.49)		1.13 (0.62, 2.05)	
Quintile 5	1.90 (1.20, 2.99)		1.27 (0.65, 2.49)	

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; PUMA, Public Use Microdata Area; ref, reference level.
[a] Adjusted for year, maternal age, proportion of the PUMA population under the poverty line ("PUMA % poverty"), proportion of PUMA residents who are non-Hispanic Black ("PUMA % Black"), and maternal education.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[d] P values for test for trend using continuous versions of categorical exposures.

3.3.3 Stratification by maternal age

Among NH Black births, there was modest evidence of interaction between maternal age and ICE ($p<0.07$) (Table A31). For teenaged mothers, there was no association between ICE and stillbirth (*p* value for trend <0.94; Table 6). In mothers aged 20-34, ICE quintile 4 vs 1 was associated with a 78% increased odds of stillbirth and ICE quintile 5 vs 1 was marginally associated with a 67% increased odds of stillbirth (*p* value for trend <0.04). In mothers aged 35+, residence in PUMAs with ICE quintile 5 vs 1 was associated with a nearly threefold increased odds of stillbirth (*p* value for trend <0.01). Additional adjustment for PUMA % HS strengthened these associations, with more than quadrupled odds of stillbirth in mothers aged 35+ for ICE quintile 5 vs 1 (Table A32).

Among NH white mothers, there was no evidence of associations between ICE and stillbirth in any age group.

Table 6: Odds ratios (95% CI) for associations between ICE and stillbirth stratified by maternal age in non-Hispanic Black and non-Hispanic White births, NYC (2009-2018)

	OR (95% CI) [b]	
	NH Black (n=221,925)	NH white (n=325,057)
Maternal age 10-19 years		
n	14,389	3,843
Quintile 1 [a]	ref	ref
Quintile 2	1.14 (0.67, 1.94)	1.08 (0.06, 18.22)
Quintile 3	1.42 (0.63, 3.22)	0.63 (0.02, 24.80)
Quintile 4	1.07 (0.32, 3.57)	0.73 (0.01, 43.12)
Quintile 5 [a]	1.42 (0.34, 5.90)	0.93 (0.01, 107.42)
Maternal age 20-34 years		
n	160,753	226,235
Quintile 1 [a]	ref	ref
Quintile 2	1.07 (0.88, 1.30)	1.07 (0.67, 1.71)
Quintile 3	1.12 (0.82, 1.55)	1.18 (0.63, 2.22)
Quintile 4	1.78 (1.17, 2.72)	1.09 (0.52, 2.29)
Quintile 5 [a]	1.67 (1.00, 2.80)	1.30 (0.56, 2.99)
Maternal age 35-63 years		
n	46,783	94,979
Quintile 1 [a]	ref	ref
Quintile 2	1.30 (0.98, 1.72)	0.86 (0.47, 1.57)
Quintile 3	1.73 (1.13, 2.60)	0.95 (0.43, 2.08)
Quintile 4	1.51 (0.79, 2.88)	1.24 (0.51, 3.01)
Quintile 5 [a]	2.70 (1.32, 5.48)	1.30 (0.48, 3.55)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[b] Adjusted for year, proportion of the PUMA population under the poverty line, proportion of PUMA residents who are non-Hispanic Black, and maternal education.

3.3.4 Post-hoc analyses

In post-hoc analyses, we explored further the associations between structural racism and stillbirth, including (1) stratifying the main models by (a) median PUMA % poverty, (b) median PUMA % Black, (c) median PUMA % HS, (d) sex, and (e) gestational age; (2) adjusting for additional individual-level covariates (maternal medical conditions, number of prenatal care visits, and insurance status); and (3) using different versions of ICE for (a) income only and (b) race only (Table A33 to Table A40).

In NH Black women, associations between ICE and stillbirth were no longer present

when stratified by median PUMA % poverty; associations between Isolation and stillbirth persisted, and were stronger in the median+ stratum (Table A33). Associations between both structural racism measures and stillbirth persisted when stratified by median PUMA % Black, but only in the <median stratum (Table A34). Similarly, associations between both measures and stillbirth persisted when stratified by median PUMA % HS, but only in the <median stratum (Table A35).

Sex-stratified models showed little difference in associations between Isolation and stillbirth, but for ICE, associations were only present for males, and this persisted with additional adjustment for individual-level covariates (Table A36). Gestational age-stratified models revealed that associations were only present in preterm births (20-36 weeks) for both exposures (Table A37). The model with additional adjustment for individual-level covariates produced a weaker OR for ICE quintile 5 vs 1 (1.68; 95% CI 1.03, 2.73) in comparison with results from the main model (Table A38).

Models using a race-only version of ICE showed no evidence of associations with stillbirth (Table A40), and models using a poverty-only version showed weaker evidence than for the ICE version using both race and poverty (the main model), although estimates were in the same direction, with an OR of 1.48 (95% CI 1.04, 2.12) for ICE quintile 4 vs 1 (Table A39).

In white women, none of these post-hoc analyses showed evidence of associations between ICE and stillbirth, but two showed evidence of associations between Isolation and stillbirth: stratification by PUMA % HS (OR of 2.20, 95% CI 1.15, 4.21, for Isolation tertile 3 vs 1 in PUMAs with educational attainment above the median (Table A35)) and stratification by sex (OR of 2.41, 95% CI 1.10, 5.31, for Isolation tertile 3 vs 1 in males (Table A36)).

3.4 Discussion

Between 2009 and 2018, the stillbirth rate in NYC was three-fold higher in NH Black families than NH white families (13.8 vs 4.7), consistent with a century of Black-white disparity in stillbirth rates. We found that structural racism as measured by ICE and Isolation was associated with stillbirth in NH Black but not NH white mothers. This would seem consistent with our hypothesis that structural racism may help to explain racial disparity in stillbirth rates; however, the associations we observed were not in the expected direction. Specifically, NH Black mothers living in PUMAs with a high concentration of privilege had 90% *greater* odds of stillbirth in comparison to those living in PUMAs with a high concentration of disadvantage (ICE quintile 5 vs 1), and NH Black mothers living in PUMAs that were the most isolated had 40% *lower* odds of stillbirth in comparison to those living in PUMAs that were the least isolated (Isolation tertile 3 vs 1). While the measures we used to reflect structural racism (ICE and Isolation) may help to explain the Black-white disparity in stillbirth rates, our results raise questions about the way they operationalize structural racism, meriting further investigation.

3.4.1 Interpretation of results

ICE and Isolation: We found that residence in PUMAs in ICE quintiles 4 and 5 vs 1 increased the odds of stillbirth for NH Black mothers. More specifically, PUMAs with relatively high concentrations of well-off white residents appear to confer a higher risk of stillbirth for NH Black mothers than do PUMAs with relatively high concentrations of low-income Black residents. The ORs for the ICE measure, indicating a 70-90% greater odds of stillbirth with residence in PUMAs of privilege in NH Black mothers, are similar in magnitude to estimates for known individual-level risk factors for stillbirth such as chronic hypertension and short interpregnancy interval.[1] Reflecting the negative correlation between the two measures of

structural racism, this result was consistent with our finding for Isolation, that tertiles 2 and 3 vs 1—representing high population concentrations of NH Black residents vs racially mixed populations—were protective against NH Black stillbirth. Together these results suggest that, after adjusting for baseline levels of poverty and % Black residents, residence in neighborhoods primarily composed of Black residents reduced the odds of stillbirth for NH Black mothers, even when (as captured by ICE) such neighborhoods also encompassed relatively higher proportions of *low-income* Black residents—and with no evidence of associations between either of these exposures and stillbirth for NH white mothers, including in the majority of sensitivity and post-hoc analyses. Post-hoc results also suggested that the effect of ICE is through combined disadvantage related to both poverty and race, rather than being driven by one or the other of these components. The consistency of these findings suggests that the effects we estimated may be real and not artefactual, but another explanation could be that the models were mis-specified (see Strengths and Limitations below). The resilience of associations between both ICE and Isolation and stillbirth in our sensitivity analyses, including models adjusting only for individual-level covariates, increased confidence in our results for these exposures. However, the direction of association we observed is not consistent with what has been observed in other studies. Following the literature, we operationalized ICE on a linear scale by which low values signify disadvantage and higher levels of structural racism, and high values represent privilege and less structural racism, and therefore our results would suggest, perversely, that higher exposure to structural racism is protective for Black mothers. However, structural racism *by definition* oppresses individuals due to their racial group membership, so such an interpretation does not make sense.

Stillbirth is just one outcome on the reproductive, maternal, neonatal and child health

(RMNCH) continuum, and as such, it has many of the same risk factors and causes as neonatal and maternal mortality and perinatal morbidities such as preterm birth and low birthweight.[44 102] Hence, while there are only two other studies on structural racism and stillbirth itself,[64 81] the subset of RMNCH literature that focuses on structural racism as an exposure is also relevant for examining our study results. Our results contrasted with three studies of ICE and perinatal outcomes in NYC which all found associations in the expected direction—with increased risk of adverse outcomes for *lower* ICE quintiles. Huynh et al. found 10-54% greater odds of preterm birth and infant mortality with greater concentrations of deprivation (lower ICE quintiles),[222] Janevic et al. found 60% greater odds of preterm morbidity/mortality in the lowest vs highest ICE quintile,[223] and Krieger et al. found nearly tripled odds of infant mortality in the lowest vs highest ICE quintile.[217] These studies did not explore variation by race, hence their estimates would reflect the directions of association that held for the majority racial groups in their study populations, which were 60-79% non-NH Black. However, this would not explain differences with our results for ICE, since our estimates of associations with stillbirth in the Black+white population were also not in the expected direction (although it would be of interest to estimate associations in a population including Hispanic births to see if results more closely approximated those in the literature).

Our results also contrast with several studies on Isolation and adverse pregnancy outcomes. In one of the two studies of stillbirth and segregation, Williams et al. found a reduced risk of stillbirth with lower Isolation in both Black and white mothers.[64] One study that adjusted for race found increased Isolation was associated with decreased birthweight and decreased gestational age,[199] and several studies found increased Isolation to be associated with adverse outcomes in Black births specifically, including decreased or low birthweight[209 240], preterm or

very preterm birth[209 230], and infant mortality[240].

Interestingly, none of the above-mentioned studies measured structural racism at a similar level to our study (PUMA). We measured exposures across 55 PUMAs with populations of about 100,000 each. Huynh et al. and Janevic et al. measured ICE at lower levels with slightly smaller average populations, including 2,168 census tracts (average population of 4,000) and 183 zip code areas (population range 10-50,000 each), respectively. In contrast, the above-mentioned studies using Isolation as the exposure all measured it at levels higher than we did—either county, hospital reference region, or metropolitan statistical area (MSA). Chambers et al. measured Isolation in 33 counties with minimum populations of 100,000 each, so similar in size to the PUMAs we used;[199] however, MSAs may have populations of several million.

Krieger et al. found that associations between ICE and assault varied depending on the level at which ICE was measured, with stronger associations between low ICE quintiles (equated to deprivation) and both assault and child mortality when ICE was computed at census tract vs city or town level.[221] Specifically, associations between ICE and child mortality in NH Black families showed that increasing disadvantage conferred risk with ICE measured at census tract level, but when ICE was measured at city level, estimates were protective (<1) and associations were no longer significant.[219] These results suggest that level and population size may both matter for directions of effect between ICE, Isolation and adverse pregnancy outcomes including stillbirth, but do little to shed light on how.

Another potential explanation for the difference in results is effect modification by degree of segregation, a possibility we did not explore in the present study. For example, one study found that increased Isolation was associated with increased risk of preterm birth and low birthweight, but only in counties with a low prevalence of these outcomes.[237] Finally, all the

studies mentioned (other than Williams et al.) are likely to have excluded stillbirths from their study populations, thereby conditioning on survival status, possibly introducing live birth bias. A study of this phenomenon modelled the effects of live birth bias on associations between exposure to PFAS and ADHD in childhood. Differing assumptions about strengths of association between PFAS and both fetal survival and ADHD were shown to result in differing degrees of bias in the PFAS-ADHD association, such as modest underestimates of the association or a reversal of the direction of effect.[241] Another modelling study of prescription drug use and preeclampsia reached similar conclusions about the possible effect of conditioning on fetal survival for the strength and direction of estimates of association.[242] Live birth bias may therefore help to reconcile the disparate findings; however this would depend on details of the associations between ICE, Isolation, and the specific pregnancy outcomes within each specific study population.

If the patterns of association we observed are not artefactual, the question remains as to why they were not in the expected direction. Our findings suggest that residence in neighborhoods with concentrations of Black residents, regardless of their wealth status, is protective against stillbirth for NH Black women, while residence in neighborhoods with concentrations of well-off white residents increases the odds of stillbirth for NH Black women. While well-off, high-white-population neighborhoods may be enriched with health, education and other services that theoretically protect against stillbirth, these services may be less accessible or of lower quality for Black mothers.[235] Several studies have found that Black women experience worse health outcomes regardless of access to healthcare; for example, Black active duty military women have a higher risk of severe maternal morbidity than their white counterparts despite shared access to the military healthcare system.[243] A study in nearly 7

million pregnant women found higher odds of severe maternal morbidity in Black than white women in every category of income, insurance, hospital patient profile, and region.[244] Other studies have found that Black women receive lower quality of care than white women.[245-248] Residing in areas of privilege is thus less protective for Black than white mothers.[236 249 250] However, to explain our findings, subpar access to resources would also need to render Black mothers in PUMAs of privilege worse off than Black mothers in PUMAs of disadvantage.

One possibility is that reproductive healthcare for NH Black women is in fact worse in privileged than disadvantaged areas. If either access to or received quality of healthcare is worse for NH Black women in privileged areas than in disadvantaged areas, the baseline quality of the healthcare itself will be less important. However, the persistence of associations between ICE and stillbirth in our post-hoc analyses after additional adjustment for individual-level covariates that may be proxies for quality of healthcare (e.g., number of prenatal care visits, insurance status) is not consistent with this explanation. Another possibility lies in the very concepts of 'privilege' and 'disadvantage'. Disadvantage for whom? Clearly a place that confers a higher risk of stillbirth is not a place of privilege for the mothers who experience stillbirth; nor is a place that protects against this risk a place of disadvantage for those same mothers. Well-off white neighborhoods are populated predominantly by residents who are natively privileged due to their race. Such neighborhoods may have fewer social and community supports for Black mothers and/or confer higher or more constant stress to NH Black mothers through a variety of pathways.[251] These could include increased rates of experiencing interpersonal racism or vicarious racism; various forms of discrimination, for example in healthcare settings, where health providers may have increased bias in comparison to providers in PUMAs with higher proportions of NH Black residents; and social isolation. In contrast, residence in PUMAs with

Isolation tertile 3—high concentrations of Black residents —could reduce the frequency of interpersonal racist encounters and provide social resources to counteract stress. A study of psychiatric disorders among native Dutch and several Dutch immigrant populations found that schizophrenia risk was significantly higher for specific immigrant populations residing in neighborhoods with lower densities of residents from the same immigrant groups after adjusting for socioeconomic level of the neighborhood, providing evidence of health benefits conferred by living in ethnic enclaves.[252] Supporting this line of reasoning, Huynh et al. found that high levels of gentrification in NYC were associated with an increased risk of preterm birth in NH Black mothers, but were protective for NH white mothers.[236]

Moreover, our finding that older NH Black mothers had higher odds of stillbirth with residence in PUMAs of "privilege" vs "disadvantage" than younger NH Black mothers is consistent with a stress pathway for this association. The weathering hypothesis predicts worsening health outcomes for Black women as they age, such that racial disparities will become more prominent with age. Our results for this maternal age stratification analysis contrasted with a recent study examining evidence for the weathering hypothesis in relation to stillbirth. Brisendine et al. found that racial disparity in stillbirth rates increased through age 34, but then declined, while we found that the greatest disparity in risk was after age 35.[153] However, they treated age as the exposure and did not investigate any other risk factors that might produce increased stress, such as our structural racism exposures.

This brings us back to the question of what the structural racism measures that we used actually mean. We have discussed above the possibility that ICE and Isolation mean different things when measured at different levels, and we have shown that they produce very different estimates of association in Black and white mothers. To what extent, however, do they represent

structural racism as conceptualized in the literature (and in our analyses)? The literature equates high Isolation (Isolation tertile 3) and low ICE (ICE quintile 1) with structural racism. The measures *are* structural; they *are* race-based; and they recognize that economic, social, and political oppression disadvantages Black individuals and advantages white individuals. It could be that, at least in this population and for this outcome, structural racism is manifesting differently at the PUMA level, as low Isolation (Isolation tertile 1) and high ICE (ICE quintiles 4 and 5), reflecting all-of-society structures and processes that together make well-off white neighborhoods and mixed-race PUMAs harmful for NH Black pregnancy outcomes relative to residence in PUMAs with high proportions of Black residents. It could also be that ICE does a poor job of codifying what 'privilege' and 'disadvantage' mean for NH Black mothers.

Dissimilarity and Educational Inequity: Our largely null findings for both race groups with Dissimilarity and Educational Inequity were another unexpected result, as again, they contrast with much of the literature. In particular they contrast with the two extant studies of segregation and stillbirth. Williams et al. found that lower Dissimilarity was protective against stillbirth in both Black and white mothers, although with a stronger protective association in Black mothers.[64] Brown et al. found that higher Dissimilarity was protective against stillbirth in white mothers and had no association in Black mothers, contrasting with our finding of no evidence for modification of associations between Dissimilarity and stillbirth by race.[81]

Other studies have also found increased risk of other adverse pregnancy outcomes with increased Dissimilarity, including low birthweight (adjusting for race),[199] infant mortality but only in white infants,[240] and very preterm birth but only in Black infants,[230] again suggesting an interaction with race, which contrasts with our null findings. Two of these studies measured Dissimilarity at the MSA level which, as mentioned above, can have significantly larger

populations than the NYC PUMAs. Consistent with the possibility that at least for this exposure, level may help to reconcile our results with the literature, another study which used census tract as the level of measurement found no evidence of an association between preterm birth and Dissimilarity.[253] However, both the studies of segregation and stillbirth used levels of analyses with similar populations to the NYC PUMAs (100,000-120,000 per unit), meaning that the choice of level would not account for the differing results for these two most relevant studies.

There was less literature using Educational Inequity than Isolation or Dissimilarity as the structural racism exposure in association with adverse pregnancy outcomes. Pabayo et al. found higher odds of both infant and neonatal mortality in Black but not white mothers residing in states with lower racial equity in educational attainment,[200] with similar findings in another study.[203]

As with Isolation, it may be that for Dissimilarity there is effect modification by degree of segregation; Brown et al. found that odds of stillbirth for Black vs white mothers were higher in high-segregation than low-segregation counties, with non-overlapping 95% CIs,[81] and one of the above-mentioned studies found that increased Dissimilarity was only associated with preterm birth and low birthweight in areas with a low prevalence of these outcomes.[237]

We did find evidence for interaction between Dissimilarity and race when using the alternative version of the Index; however, race-stratified analyses showed only modest evidence of an association in NH Black mothers (only for tertile 2 vs 1), and no association in NH white mothers. Similarly, a sensitivity analysis stratifying by ACS vintage showed modest evidence of a protective association between greater Educational Inequity and stillbirth in NH Black but not white mothers for vintage 2013 only. The lack of any other evidence for associations between these exposures and stillbirth in our study sample suggests these results may have been

anomalies. However, the fact that we found differences for Dissimilarity depending on which formula we used calls into question whether the different versions are truly measuring the same underlying construct, an area worthy of further examination, given how commonly-used this measure is.

3.4.2 Strengths and limitations

Our study sample was relatively large, rendering the number of Black and white stillbirths sufficient to investigate associations with structural exposures that may not have strong effect sizes. We conducted multiple sensitivity analyses to assess robustness of results. We faced several limitations. The design is cross-sectional; while reverse causality was not possible, our inability to account for length of exposure may have caused a bias to the null, if longer exposure to structural racism increases the odds of stillbirth. The use of two data sources to estimate exposures (for 2009-2013, a period that included the year that NYC introduced a more comprehensive fetal death reporting procedure, and 2014-2018) may have introduced non-differential measurement error, biasing results toward the null. U.S. Census undercounting of individuals may be differential across race, introducing measurement error.[227] Sibling clustering could not be adjusted for, likely causing a bias away from the null. We attempted to address this issue by sensitivity analyses in single years of data, but results were inconclusive. Individual- and PUMA-level education may be mediators rather than confounders, possibly resulting in mis-specified models. Adjusting for these covariates would produce less-biased estimates of the total effect (if they are confounders) or less-biased estimates of the direct effect (if they are mediators). While both types of estimates are of interest, our intent was to estimate the former. A related issue was the correlation between PUMA-level covariates, as adjusting could result in overcontrol. Sensitivity analyses adjusting only for individual-level covariates produced a

weaker adjusted OR for ICE quintile 5 vs 1 in Black births (the OR was reduced from 1.90 to 1.36) and a non-significant but flipped direction of association for ICE quintile 5 vs 1 in white births. Results of this sensitivity analysis for Isolation tertile 3 vs 1 in Black births were consistent with our main model (the adjusted OR weakened slightly from 0.60 to 0.67), and in white births, the adjusted OR did not change, but the 95% CI excluded the null value (Table A23). Post-hoc analyses in Black births suggest that PUMA % poverty does confound associations between ICE and stillbirth, but may be an effect modifier for associations between Isolation and stillbirth, while PUMA % Black and PUMA % HS may be effect modifiers for both exposures; this suggests that further study should build different models for associations between these two exposures and stillbirth.

3.4.3 Further study

We focused on racial disparity in stillbirth rates between NH Black and NH white births, but other groups are also affected by racism. In particular, we found that Hispanic and Native American mothers in NYC have increased rates of stillbirth compared with NH white mothers, as do mothers whose race data were missing. The role of structural racism in these disparities also deserves study. The results of our secondary analysis investigating the weathering hypothesis suggested that structural racism and stillbirth in NH Black births could potentially be linked by a stress pathway, so it would be helpful to explore further the post-hoc analyses that demonstrated some effect modification by sex and gestational age. There is evidence that associations between maternal stress and adverse pregnancy outcomes vary by sex[254], and maternal stress is a risk factor for preterm birth;[71] moreover, our bivariate analyses showed that sex-specific and gestational age-specific stillbirth rates vary by race. Researchers should investigate causes of variation in SBRs by borough: what makes Staten Island riskier than the

Bronx for NH Black mothers? Potentially modifiable factors associated with lower stillbirth risk in PUMAs within each borough should be identified. It would be useful to explore whether and how structural racism is associated with stillbirth in other areas of the U.S., assessing whether our results might be generalizable to other large, diverse metropolitan areas. We also plan to use the results from our primary models to inform further development of continuous versions of the exposures, potentially including the use of splines or quadratic terms, to better model associations between these structural racism measures and stillbirth. Finally, given some of our unexpected results, further sensitivity analyses, including building borough-level structural racism measures from PUMA-level data, investigating reasons for the differing results for Isolation for the main and alternative versions of this exposure, systematically reviewing the literature for research that has found or discussed directions of association for Isolation and ICE similar to those we found, and examining other domains of structural racism, would also be of interest.[255]

3.4.4 Conclusion

We present evidence that NH Black mothers in NYC are at greater risk of stillbirth in PUMAs with relatively higher concentrations of well-off, white residents vs low-income, Black residents, with residence in mostly-Black resident neighborhoods reducing the odds of stillbirth by 40% for these mothers. Since we found no associations between either of these measures and stillbirth in NH white mothers, the results may help to explain Black-white disparity in stillbirth rates in NYC. However, the associations between both ICE and the Index of Isolation and stillbirth were not in the expected direction for NH Black mothers, raising questions about how well these measures (as they are usually defined and interpreted) capture structural racism, and suggesting further lines of inquiry. Mechanisms by which ICE and Isolation are associated with

stillbirth are unknown, but one possibility is a stress pathway. However it is codified, structural racism appears to comprise a meaningful component of the complex story of why stillbirth happens relatively more often to NH Black mothers—a story which includes but goes beyond individual-level risk factors.

Chapter 4: Does methylation of stress-related genes mediate associations between maternal stress and stillbirth?

4.1 Introduction

Stillbirth (fetal death at 20+ gestational weeks) is a major public health burden in the United States. The stillbirth rate is 5.7 per 1000 total births, and has been worse than the infant mortality rate in the U.S. (4.0 per 1000) for decades.[2 20] The U.S. stillbirth rate is also worse than that of 31 other high-income countries.[10 44] There is large variation in stillbirth rates by race, with a stillbirth rate in non-Hispanic Black families of 10.4 per 1000 that is more than twice as high as the rate in non-Hispanic white families.[1 2] One-third of stillbirths are unexplained,[2 9 58-61] and knowledge of mechanisms is insufficient.[4 102] Limited understanding of causes at all levels reduces opportunities for prevention.[7 8]

Maternal stress (hereafter "stress") holds promise as a plausible component cause of stillbirth. There is substantial evidence for a connection between stress and many adverse health outcomes[68-72] through physiological and behavioral pathways.[68 69 73 75 78 79 83] Adverse pregnancy outcomes[69] associated with stress include preeclampsia, low birthweight,[256] intrauterine growth restriction,[257] and preterm delivery,[1 70 71 258-260] each of which is associated with a higher risk of stillbirth.[68 73 79] There is also some evidence linking stress to stillbirth.[73] Three U.S. studies found that adverse childhood experiences[74 75] and significant life events were associated with increased odds of stillbirth,[76] and four large European cohort studies found that high perceived stress, bereavement, and unemployment were associated with an increased risk of stillbirth.[77-80]

A causal relationship between stress and adverse pregnancy outcomes is biologically plausible through physiological impairment of stress responses, leading to inflammation and

reducing fetal defenses.[68 73 78 79] One approach to increasing confidence that the association is causal is to acquire evidence of a biological mechanism. One possible mechanism is DNA methylation, an epigenetic modification that occurs when a methyl group attaches to a cytosine base that is followed by a guanine base (a CpG), thereby often preventing transcription factors from binding at that genomic location, and hence often repressing transcription and translation of the associated proteins.[100] Therefore, methylation of stress-related genes may adversely affect stress responses. Many stress-related genes are highly expressed in the placenta, and placental methylation has been associated both with adverse prenatal exposures such as stress and with adverse fetal outcomes.[261-267] A systematic review of adverse maternal exposures, perinatal outcomes, and methylation of three such genes, *NR3C1*, *HSD11B1*, and *HSD11B2*, found that methylation may mediate the stress to birthweight pathway.[100] Two small studies examined methylation in relation to pregnancy loss including stillbirth. Pliushsh et al. found modest evidence for unadjusted associations between pregnancy loss, including miscarriage and stillbirths at 21-42 weeks, and hypermethylation of the imprinting control regions of six imprinted genes including *H19;* two stillbirths also displayed loss of imprinting (biallelic expression) in the reciprocally imprinted gene *IGF2*.[268] Vasconselos et al. examined six imprinted genes in relation to unexplained pregnancy losses including early stillbirths up to 24 weeks, finding increased expression of *IGF2* in placental tissue in unadjusted analyses.[269] However, there has been no research on methylation as a mediator of associations between stress and stillbirth.[115]

Using the well-phenotyped stillbirths and livebirths of the population-based U.S. Stillbirth Collaborative Research Network (SCRN) case-control study, we examined whether: 1) stress is associated with stillbirth, 2) stress is associated with placental methylation of stress-

related genes, 3) placental methylation of stress-related genes is associated with stillbirth, and 4) associations between stress and stillbirth are mediated by methylation of stress-related genes.

4.2 Methods

4.2.1 Study design

This was a case-control study embedded in the SCRN.

4.2.2 Data source and study sample

The U.S. National Institute for Child Health and Human Development established the Stillbirth Collaborative Research Network (SCRN) in 2003 to explore causes of stillbirth in the United States.[270] The SCRN was the source of all data used in this study. SCRN was a population-based case-control study of 2,703 stillbirths and livebirths. Screening for SCRN occurred between 2006 and 2008 at the 59 hospitals covering ≥90% of all stillbirths and livebirths in five catchment areas: Rhode Island and Bristol County, Massachusetts (Brown University); DeKalb County, Georgia (Emory University); Galveston and Brazoria Counties, Texas (University of Texas Medical Branch at Galveston, UTMB); Bexar County, Texas (University of Texas Health Sciences Center at San Antonio, UTHSC); and Salt Lake County, Utah (University of Utah Health Sciences Center). All stillbirths (fetal deaths of 20+ completed gestational weeks), all livebirths of 20-23 weeks, and a subset of livebirths of 24+ weeks were eligible. Inclusion criteria were maternal age ≥13 years and identification prior to hospital discharge. Exclusion criteria were induced abortion, incarceration, and inability to consent. 2,595 mothers were enrolled at delivery, with written consent (or assent for minors) obtained from all participants.[270]

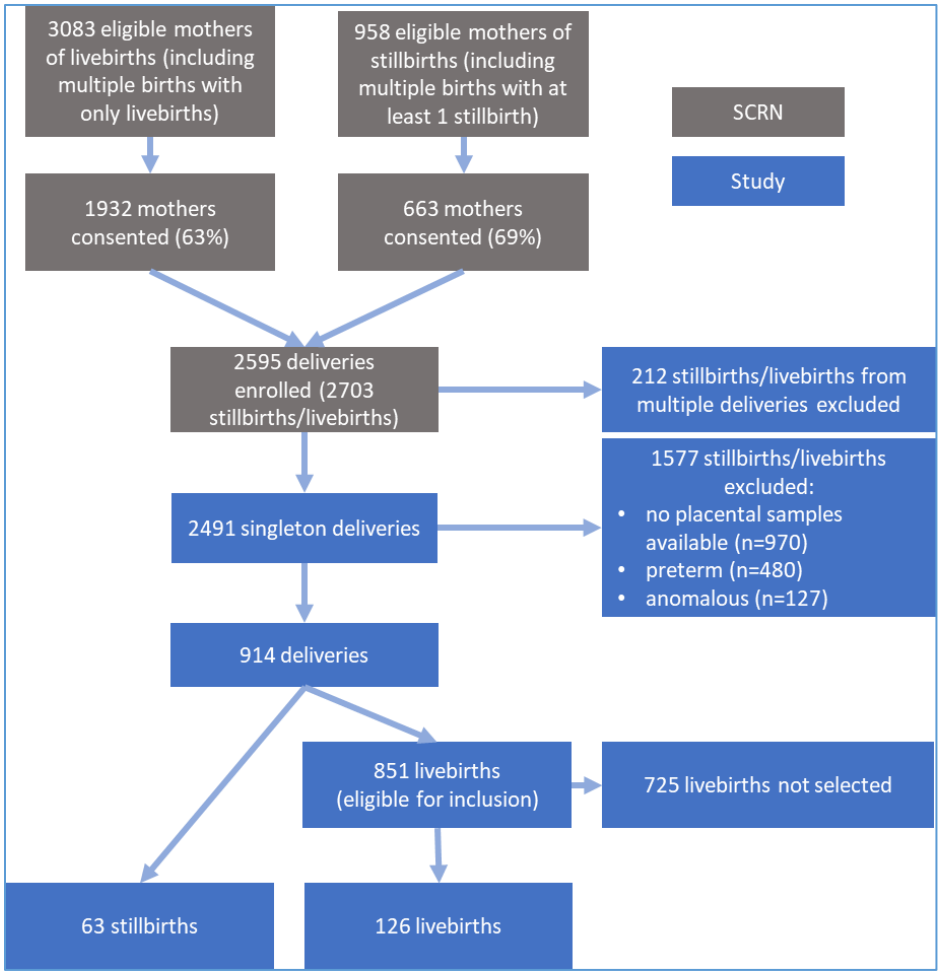

Figure 11: Selection of study stillbirths/livebirths from the Stillbirth Collaborative Research Network (SCRN)

Maternal interviews were conducted in person in English or Spanish in the hospital soon after delivery, or by phone within four weeks. Over 90% of mothers agreed to interviews, biospecimens, and medical record abstraction; 99% of stillbirth mothers and 93% of livebirth mothers agreed to placental examination; and 84% of stillbirth mothers agreed to a postmortem examination.[57] For this study, the sample comprised all 63 full-term (37+ weeks) singleton stillbirths with available placental biospecimens and no identified anomaly as well as 126 full-term singleton livebirths with available placental biospecimens. Livebirths were selected using simple random sampling without replacement, and frequency matching to stillbirths by

catchment area. Figure 11 shows the relationship between SCRN and the study sample of 189 stillbirths/livebirths.

4.2.3 Exposures

The construct of interest was maternal stress; however, since SCRN data do not include measures of perceived stress, we used measures of hypothesized stressors as proxies (hereafter "stressors"). These were an index of significant life events (SLE) and an index of socioeconomic disadvantage (Disadvantage). The significant life events are from the CDC's Pregnancy Risk Assessment Monitoring System (Box 1).[271] In SCRN interviews, mothers were asked whether any of 13 significant life events had occurred to them in the 12 months prior to birth; we then summed these for an SLE range of 0 to 13.[270] The significant life events are usually grouped into four 'factors' as noted in Figure 12,[272-277] including in previous work in the SCRN cohort.[76]

Financial Factor

1. "My husband or partner lost his job"
2. "I lost my job even though I wanted to go on working"
3. "I had a lot of bills I couldn't pay"

Emotional Factor

1. "I moved to a new address"
2. "I was homeless"
3. "My husband or partner or I went to jail"

Traumatic Factor

1. "A close family member was very sick and had to go into the hospital"
2. "Someone very close to me died"

Partner-related Factor

1. "I got separated or divorced from my husband or partner"
2. "I argued with my husband or partner more than usual"
3. "My husband or partner said he didn't want me to be pregnant"
4. "I was in a physical fight"
5. "Someone very close to me had a bad problem with drinking or drugs"

Figure 12: Significant Life Events

The second stressor measure, following Appleton et al. and Miller et al., captures socioeconomic disadvantage.[263 278] Five relevant variables available in SCRN were dichotomized (with 'present' scored as 1) and summed to obtain a Disadvantage score between 0 and 5. The five hypothesized stressors included in this Index are maternal education <12 years, living in public housing or shelter or being homeless, family income in the past 12 months only from public or private assistance, no insurance for prenatal care, and not cohabiting with a partner. Because non-cohabitation could be an advantage rather than a disadvantage, in a sensitivity analysis we used a modified version of Disadvantage that excludes partnership status. We used categorical versions of each Index for the primary analyses (0, 1, 2, 3, or 4+ SLE events and 0, 1, or 2+ Disadvantage items), based on distributions of the indices in SCRN; see Appendix B.

4.2.4 DNA methylation assay

Methylation data were obtained using DNA extracted at the University of Utah from SCRN placental samples that had been frozen at delivery. After extraction, DNA quantity and quality were tested, and samples normalized to address differential concentrations across cells that could bias results. Bisulfite conversion was then performed. This is a process whereby unmethylated cytosine bases are converted to uracil, leaving the methylated cytosine bases unchanged and available for detection. The 189 samples were then loaded onto two plates for processing. To minimize the chance of confounding by batch effect (differential methylation by location of samples during processing), we provided the University of Utah with prespecified plate locations for each sample (Table A46). Processing used Illumina's MethylationEPIC microarray which is able to identify the methylation status of about 850,000 CpGs. These comprise just 3% of the 28 million CpGs in the human genome, but cover many key genomic regions. During processing, one sample received multiple quality control flags indicating

inefficient bisulfite conversion (less converted DNA available for methylation processing), so we excluded it in a sensitivity analysis.

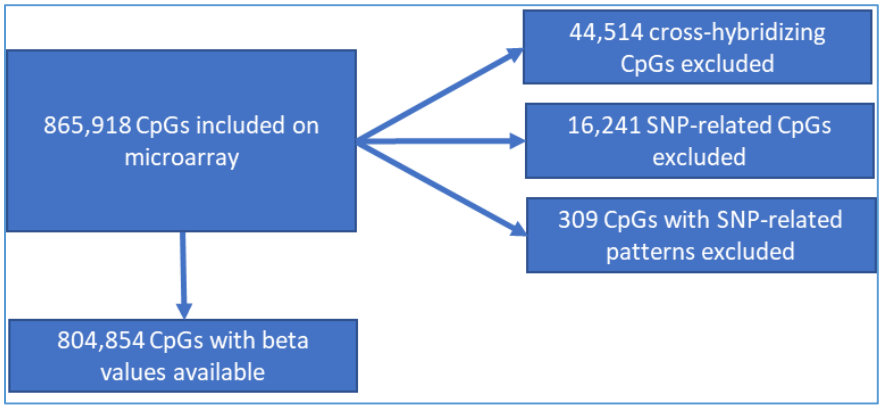

Figure 13: Flowchart showing number of CpGs available for analyses

Abbreviations: CpG, cytosine-guanine base pair; SNP, single nucleotide polymorphism.

The raw data produced by the microarray were transformed into beta values. A beta value of 0 for a given CpG means that none of the copies of that CpG were methylated, and a beta value of 1 means that all the copies were methylated. Other standard quality control checks and pre-processing steps were then performed. We identified six sex mismatches (all livebirths—three from Brown, three from Utah—which we subsequently excluded from all analyses) and two outliers (excluded in a sensitivity analysis). Principal component analysis was performed on methylation beta values and regression of the first two principal components onto plate yielded evidence of an association ($p<0.05$); hence we adjusted for plate in all analyses. Because DNA samples contain a mixture of cell types, each with a different methylation profile, cell type must be adjusted for in methylation analyses; hence we estimated cell type proportions for each of the 189 placental samples (Table A47). The final dataset contained beta values for 804,854 CpGs representing 93% of the CpGs interrogated by the microarray (Figure 13). See Appendix B for further details on production of methylation data.

4.2.5 Selection of candidate genes and CpGs

We selected five candidate genes whose methylation might mediate associations between stress and stillbirth based on a non-systematic literature review of stress-related genes previously associated with adverse pregnancy outcomes. These were *BDNF*, *FKBP5*, *HSD11B2*, *IGF2*, and *NR3C1* (Table A48 and Appendix B). Methylation of placental *BDNF*, a gene involved in regulation of the stress response and mood disorders, has been found to be associated with both war trauma and chronic stress.[279 280] Hypermethylation of placental *FKBP5* has been associated with maternal distress, depression and PTSD.[281] Lower maternal education and increased cumulative risk have been associated with hypomethylation of placental *HSD11B2*, which protects the fetus from exposure to maternal glucocorticoids by converting cortisol to cortisone.[263 282 283] Maternal stress has also been associated with placental *IGF2* methylation, an imprinted gene that plays a role in fetal growth.[268 282 284-288] Increased chronic stress and decreased birthweight have been associated with hypomethylation of *NR3C1*, which encodes the glucocorticoid receptor.[289] See Table 7 for basic data on these genes and Table A49 for details. We selected CpGs on gene bodies or on promoters and enhancers upstream or downstream of gene bodies for our analyses, as these are regions critical for gene functioning. Of the 865,918 CpGs interrogated by the microarray, 1,217 were in one of these regions of interest for the five candidate genes, of which beta values were available for 1,191 (98%) (Table A50).

Table 7: Summary of the five candidate genes: *BDNF*, *FKBP5*, *HSD11B2*, *IGF2* and *NR3C1*: Location, functions, placental expression, and number of studies with stress measures and birth outcomes with types of tissues studied

	BDNF	***FKBP5***	***HSD11B2***	***IGF2***	***NR3C1 (GR)***
Name	Brain-derived neurotrophic factor	FKBP Prolyl Isomerase 5	Hydroxysteroid 11-Beta Dehydrogenase 2	Insulin-Like Growth Factor 2	Nuclear Receptor Subfamily 3 Group C Member 1
Location [a]	Chr 11: 27,654,893-27,722,058	Chr 6: 35,573,585-35,728,583	Chr 16: 67,430,652-67,437,553	Chr 11: 2,129,112-2,149,566	Chr 5: 143,277,931-143,435,512
Length (bp) [a]	67,166	154,999	6,902	20,455	157,582
Functions	encodes a protein involved in neural, placental and fetal development[279 290]	encodes glucocorticoid receptor co-chaperone protein (*FKBP51*)[291]	converts cortisol into cortisone[266 292]	encodes a protein involved in fetal growth[269 282 287 293 294]	encodes glucocorticoid receptor (GR)[292 295]
Placental expression	low to moderate[296-298]	low to moderate[281 299-302]	highly expressed in at least one cell type in the placenta	highly expressed in at least one cell type in the placenta	highly expressed in most cell types in the placenta
# studies with stress (stressor measures)	4 (Everyday Discrimination Scale[290]; Parental Bonding Instrument[303]; neighborhood socioeconomic disadvantage[304]; chronic stress and war trauma[279])	6 (Perceived Stress Scale[281]; Prenatal Distress Questionnaire[281]; Childhood Trauma Questionnaire[291]; Everyday Discrimination Scale[290]; child and adult socioeconomic status and social mobility based on education[305]; neighborhood socioeconomic disadvantage[304]; chronic stress and war trauma[289])	3 (Perceived Stress Scale[281]; Prenatal Distress Questionnaire[281]; prenatal socioeconomic adversity: maternal education, poverty, dwelling crowding, tobacco use and cumulative risk[263]; depression or anxiety during pregnancy[306])	3 (Perceived Stress Scale[282]; State-Trait Anxiety Inventory[282]; Edinburgh Depression Scale[288]; Pregnancy-Related Anxiety Questionnaire[288]; Life Experience Interview[282]; war trauma and chronic stress[287])	11 (Perceived Stress Scale[281 307]; State Trait Anxiety Inventory[262]; Prenatal Distress Questionnaire[281]; Childhood Trauma Questionnaire[308]; Everyday Discrimination Scale[290]; Pregnancy-Related Anxiety Questionnaire[262]; Maternal Fetal Attachment Scale[262]; depression/anxiety during pregnancy[306]; chronic psychosocial stress[309]; early life stress[310]; material deprivation, daily psychosocial stress, war stress[295]; neighborhood socioeconomic disadvantage[304]; chronic stress and war trauma[289])
Among studies with stress measures, # with birth outcomes (outcomes)	0	2 (fetal coupling[281], birthweight[289])	2 (fetal coupling[281], infant neurobehavior[306])	1 (birthweight[287])	4 (fetal coupling[281], infant neurobehavior[306], birthweight[289 295])

	BDNF	***FKBP5***	***HSD11B2***	***IGF2***	***NR3C1 (GR)***
# studies with birth outcomes only (outcomes)	0	0	3 (birthweight[265 266], gestational age[265], ponderal index[265 266], length[265], intrauterine growth restriction[265 266], infant neurobehavior[292])	2 (2nd trimester fetal loss[269], placental size[294], birthweight[294])	2 (infant neurobehavior[292], birthweight[311])
Tissues (# studies)	placenta (1)[279], blood (4)[279 290 303 304]	placenta (2)[281 289], blood (4)[289 290 304 305], saliva (1)[291]	placenta (6)[263 265 266 281 292 306]	placenta (3)[269 282 287], blood (3)[287 288 294], fetal tissue (1)[269]	placenta (6)[281 289 292 306 309 311], blood (9)[262 289 290 295 304 307-310], saliva (2)[309 310]

Abbreviations: bp, base pairs; Chr, chromosome.
[a] Build 38 used.

4.2.6 Analytical approach

Summary of approach: After summarizing the stressors and other covariates, we first assessed evidence for associations between stressors and stillbirth in the study sample. Second, we screened the 1,191 CpGs to identify those that are differentially methylated with respect to both stressors and stillbirth. We also identified differentially methylated regions (DMRs) on the five candidate genes. DMRs are groups of CpGs that are physically close and have similar associations with the exposure or outcome in question. DMRs were represented in analyses by the average of the beta values of their constituent CpGs.[312] Third, we carried out mediation analyses on the screened CpGs and DMRs one CpG or DMR at a time. We used categorical versions of the exposures for the primary analyses, following a prior study on stress and stillbirth in this study population, and literature which gives evidence of dose-response relationships between stressors, methylation, and perinatal outcomes (e.g., [71 74 76 313 314]). We also report results from models using continuous versions of the exposures in Appendix A. In further studies, we will use results from our primary analyses to inform development of these models (using the continuous versions of the exposures).

Associations between stressors and stillbirth: *Primary analyses*: We used logistic regression to estimate associations between stressors (measured by SLE and Disadvantage) and stillbirth in the study sample of 63 stillbirths and 120 livebirths (the six sex mismatches were excluded from all analyses). We exponentiated estimates to produce odds ratios (ORs) for stillbirth[315] and 95% confidence intervals (CIs), and reported *p*-values for the Wald test for linear trend. Unweighted data were used throughout, and due to very low missingness for most covariates, we did not impute missing values.

The following covariates were included in all models: site (a matching covariate);

maternal age (continuous), which is a risk factor for stillbirth that may also be associated with stress; and race, which is associated with disadvantage (including components of both the Index of Disadvantage and SLE) as well as with stillbirth. The reasons for the association between race and stillbirth remain unclear;[1] one hypothesis is that race group membership interacts with structural racism over the lifecourse to increase the risk of stillbirth through many pathways, both mediated by and independent of stress, including material deprivation, pre-existing and gestational conditions, pregnancy complications, prior adverse pregnancy outcomes, and access to and quality of healthcare. The SCRN dataset does not include measures of racism, so we employed race group membership as a proxy for the hypothesized joint effect of race and racism. The hypothesized associations are shown in Figure A8. Several of the Disadvantage items (for instance, income and housing status) may be associated with SLE, and (independently of stressors captured in the SLE Index) are also associated with stillbirth. Thus, for models using SLE as the exposure, we further adjusted for Disadvantage.

Sensitivity analyses: We carried out three sensitivity analyses:

- We tested associations between stress and stillbirth in a subset (n=180) of the study sample that excluded the two outliers (both stillbirths, from Utah and UTHSC) and the sample that had received multiple quality control flags during bisulfite conversion (a stillbirth from UTHSC).
- We tested associations between Disadvantage and stillbirth using a modified version of Disadvantage that excludes partnership status.
- We tested associations between stress and stillbirth in the 1,479 full-term singleton non-anomalous stillbirths (n=93) and livebirths (n=1,386) from which the study sample was drawn, in order to assess whether there was evidence of selection bias (the study sample

not being representative of the original sample). Of note, our 63 study stillbirths comprised 68% of the 93 full-term singleton non-anomalous stillbirths in the original SCRN sample (the others could not be included in our study sample due to unavailability of placental tissue).

We compared ORs and their CIs from primary and sensitivity analyses. Similar ORs with substantially overlapping CIs would suggest that selection of stillbirths and livebirths from SCRN was not affected by selection bias, and that subsequent analyses using the primary analysis model and study sample (n=183) were appropriate.

Screening of 1,191 CpGs: *Screening Step 1*: We used the formula $\mathbf{log_2}\left[\frac{\boldsymbol{\beta}}{\mathbf{1-\boldsymbol{\beta}}}\right]$ to transform methylation beta values (β) into M-values. β values (which approximate the proportion of CpG copies in one sample that are methylated) are generally easier to interpret than M-values; M-values are preferred when methylation is modelled as a regression outcome, since they are generally more normally distributed and homoscedastic. To identify CpGs that were differentially methylated with respect to stressors or stillbirth, M-values for the 1,191 CpGs were treated as individual outcomes in linear regression (stressor was the exposure) and individual exposures in logistic regression (stillbirth was the outcome). In addition, the R package DMRcate was used to identify DMRs; it works by first identifying differentially methylated CpGs and then using these to identify DMRs. To control for multiple comparisons, *p*-values were adjusted using the False Discovery Rate (FDR), and CpGs and DMRs were considered to be differentially methylated in relation to either stressors or stillbirth if adjusted *p*-values were <0.20.[261 262 279 289 292 308 316] All models were adjusted for site, maternal age,[317] cell type composition (five continuous covariates), plate, and race (Figure A8). In models for associations

between methylation and stillbirth, we also adjusted for sex, because it is associated with methylation[318 319] and stillbirth[320].

Screening Step 2: In the subset of CpGs and DMRs identified in Step 1, we produced estimates of association between stress and methylation, and between methylation and stillbirth, using linear and logistic regression, respectively. We extracted the constituent CpGs in each DMR from DMRcate output, calculated Pearson correlation coefficients for their β values, and calculated average β values for each DMR for use in subsequent analyses.[285 294] For linear regression, we used methylation M-values, transforming regression coefficients into mean differences in beta values using Kruppa et al.'s intercept method and multiplying by 100.[321 322] Regression coefficients could thus be interpreted as the mean difference in percentage methylation with each unit increase in stressor level. Because this transformation does not preserve the direction of association, we also reported the untransformed regression coefficients. For logistic regression, we used 100*β values; after exponentiating regression coefficients, odds ratios could thus be interpreted as the odds of stillbirth with a one-percentage point increase in methylation. The social construct of race has been shown to be associated with epigenetic modifications including methylation[323], related for instance to perceived discrimination[324], which could include pathways mediated by stress as well as by maternal medical conditions and other epigenetic mechanisms. As with associations between stressors and stillbirth, we adjusted for race in associations between stressors and methylation, and between methylation and stillbirth, as a proxy for the hypothesized joint effect of race and racism. We sought CpGs and DMRs with evidence of associations with *both* stress *and* stillbirth with a threshold of uncorrected *p*-values < 0.05.

Screening Step 3: To identify possible mediators of associations between stress and stillbirth, that is, mechanisms by which increased stress could increase the risk of stillbirth, we used the results from Step 2 and screened out CpGs and DMRs for which directions of association with stress and stillbirth were opposing. See Appendix B for a comment on the rationale for this step.

Mediation analyses: We reported Pearson correlation coefficients and mean methylation beta values for all CpGs and DMRs that passed the above screening steps (the mediator candidates), and then tested them for evidence of mediation in separate models (one per mediator candidate) using the R package 'Mediation', which takes a causal mediation approach.[325 326] Covariates were the same as those in Step 1 above. Linear and logistic regression used M-values. We interpreted an uncorrected *p*-value <0.05 for the average causal mediation effect (ACME) as evidence of mediation. We reported the average proportion of the effect mediated (PME) with associated *p*-values for each mediator candidate.

4.2.7 Ethics

This study was determined to be exempt by the Columbia University Human Research Protection Office Institutional Review Board.

4.2.8 Software

Other than selection of controls (SAS 9.4), all analyses were done in R.

4.3 Results

4.3.1 Descriptive analysis

Mothers in the study sample were more likely to be non-Hispanic white than mothers in SCRN (49.2% vs 40.9% for mothers of stillbirths and 47.5% vs 39.5% for mothers of livebirths)

(Table 8). Livebirths in the study sample were more likely to have occurred at Brown (27.5% vs 19.3%) or Utah (32.5% vs 23.7%) than livebirths in SCRN. Other characteristics were similar for stillbirths and livebirths in the study sample and SCRN. Missingness was low (Figure A9).

Table 8: Characteristics of stillbirths/livebirths and mothers in study sample (n=183) and SCRN (n=1,479), including Indices of Significant Life Events and Disadvantage

	Stillbirths		Livebirths	
Characteristic	**SCRN (n=93)**	**study (n=63)**	**SCRN (n=1386)**	**study (n=120)**
Stillbirth/livebirth characteristics				
Sex, n (%)				
Male	45 (48.4)	30 (47.6)	694 (50.1)	60 (50.0)
Female	47 (50.5)	33 (52.4)	692 (49.9)	60 (50.0)
Missing	1 (1.1)	0	0	0
Birthweight (grams), mean (SD)	3252.0 (618.2)	3268.4 (571.5)	3364.0 (446.2)	3468.6 (440.5)
Missing	2 (2.2)	2 (3.2)	32 (2.3)	2 (1.7)
Gestational age (weeks), mean (SD)	38.9 (1.5)	38.6 (1.4)	39.3 (1.2)	39.3 (1.1)
Site, n (%)				
Brown	22 (23.7)	18 (28.6)	267 (19.3)	33 (27.5)
Utah	27 (29.0)	21 (33.3)	329 (23.7)	39 (32.5)
UTHSC	20 (21.5)	12 (19.0)	397 (28.6)	24 (20.0)
UTMB	11 (11.8)	8 (12.7)	102 (7.4)	16 (13.3)
Emory	13 (14.0)	4 (6.3)	291 (21.0)	8 (6.7)
Maternal characteristics				
Age at delivery (years), mean (SD)	27.5 (6.6)	28.4 (6.5)	27.1 (6.1)	27.5 (5.9)
Race/ethnicity, n (%)				
White non-Hispanic	38 (40.9)	31 (49.2)	547 (39.5)	57 (47.5)
Black non-Hispanic	18 (19.4)	10 (15.9)	252 (18.2)	11 (9.2)
Hispanic	31 (33.3)	17 (27.0)	493 (35.6)	44 (36.7)
Other	6 (6.5)	5 (7.9)	94 (6.8)	8 (6.7)
Pre-pregnancy BMI (kg/m²), mean (SD) [e]	27.3 (7.0)	26.6 (6.1)	26.3 (6.5)	25.4 (5.9)
Missing	3 (3.2)	2 (3.2)	37 (2.7)	1 (0.8)
Start of prenatal care				
Trimester 2-3 or no prenatal care	16 (17.2)	8 (12.7)	194 (14.0)	15 (12.5)
Trimester 1	69 (74.2)	49 (77.8)	1129 (81.5)	101 (84.2)
Missing	8 (8.6)	6 (9.5)	63 (4.5)	4 (3.3)
Smoke exposure, n (%) [a]				
Yes	26 (28.0)	17 (27)	247 (17.8)	24 (20.0)
No	55 (59.1)	38 (60)	872 (62.9)	74 (61.7)
Missing	12 (12.9)	8 (13)	267 (19.3)	22 (18.3)
Prior stillbirth, n (%)				
Yes	6 (6.5)	2 (3.2)	16 (1.2)	1 (0.8)
No	54 (58.1)	42 (66.7)	974 (70.3)	89 (74.2)
Missing	33 (35.5)	19 (30.2)	396 (28.6)	30 (25.0)
Pregnancy complications, n (%) [b]				
Yes	59 (63.4)	39 (61.9)	616 (44.4)	45 (37.5)
No	34 (36.6)	24 (38.1)	740 (53.4)	73 (60.8)
Missing	0	0	30 (2.2)	2 (1.7)
Maternal gestational conditions, n (%) [d]				
Yes	55 (59.1)	39 (61.9)	785 (56.6)	68 (56.7)
No	18 (19.4)	11 (17.5)	255 (18.4)	26 (21.7)
Missing	20 (21.5)	13 (20.6)	346 (25.0)	26 (21.7)

Characteristic	Stillbirths		Livebirths	
	SCRN (n=93)	study (n=63)	SCRN (n=1386)	study (n=120)
Pre-existing maternal conditions, n (%) [c]				
Yes	51 (54.8)	35 (55.6)	598 (43.1)	51 (42.5)
No	34 (36.6)	23 (36.5)	710 (51.2)	63 (52.5)
Missing	8 (8.6)	5 (7.9)	78 (5.6)	6 (5.0)
Index of Significant Life Events				
Events, mean (SD)	2.3 (2.2)	2.3 (2.2)	2.0 (1.9)	1.8 (1.7)
Events, n (%)				
4+ SLE	19 (20.4)	14 (22.2)	240 (17.3)	20 (16.7)
3 SLE	11 (11.8)	6 (9.5)	157 (11.3)	13 (10.8)
2 SLE	19 (20.4)	12 (19.0)	262 (18.9)	20 (16.7)
1 SLE	18 (19.4)	12 (19.0)	337 (24.3)	33 (27.5)
0 SLE	18 (19.4)	13 (20.6)	326 (23.5)	30 (25.0)
Missing	8 (8.6)	6 (9.5)	64 (4.6)	4 (3.3)
Components of Significant Life Events Index				
Financial factor, n (%)				
Yes	28 (30.1)	20 (31.7)	381 (27.5)	29 (24.2)
No	56 (60.2)	37 (58.7)	919 (66.3)	83 (69.2)
Missing	9 (9.7)	6 (9.5)	86 (6.2)	8 (6.7)
Emotional factor, n (%)				
Yes	39 (41.9)	24 (38.1)	531 (38.3)	46 (38.3)
No	46 (49.5)	33 (52.4)	787 (56.8)	68 (56.7)
Missing	8 (8.6)	6 (9.5)	68 (4.9)	6 (5.0)
Traumatic factor, n (%)				
Yes	35 (37.6)	25 (39.7)	523 (37.7)	51 (42.5)
No	50 (53.8)	32 (50.8)	798 (57.6)	65 (54.2)
Missing	8 (8.6)	6 (9.5)	65 (4.7)	4 (3.3)
Partner factor, n (%)				
Yes	37 (39.8)	23 (36.5)	512 (36.9)	33 (27.5)
No	48 (51.6)	34 (54.0)	806 (58.2)	82 (68.3)
Missing	8 (8.6)	6 (9.5)	68 (4.9)	5 (4.2)
Index of Disadvantage				
Items, mean (SD)	0.8 (1.0)	0.7 (0.9)	0.5 (0.8)	0.4 (0.7)
Items, n (%)				
2+ items	18 (19.4)	12 (19.0)	186 (13.4)	10 (8.3)
1 item	28 (30.1)	19 (30.2)	310 (22.4)	31 (25.8)
0 items	47 (50.5)	32 (50.8)	890 (64.2)	79 (65.8)
Components of Disadvantage Index				
Maternal education, n (%)				
<12 years	23 (24.7)	14 (22.2)	255 (18.4)	17 (14.2)
12+ years	61 (65.6)	43 (68.3)	1066 (76.9)	99 (82.5)
Missing	9 (9.7)	6 (9.5)	65 (4.7)	4 (3.3)
Housing status, n (%)				
Public housing/ shelter/ homeless	14 (15.1)	10 (15.9)	94 (6.8)	6 (5.0)
Live with others (not public housing)	16 (17.2)	12 (19.0)	237 (17.1)	14 (11.7)
Rent/own	54 (58.1)	34 (54.0)	995 (71.8)	97 (80.8)
Missing	9 (9.7)	7 (11.1)	60 (4.3)	3 (2.5)
Family income source, n (%)				
Only public/private assistance	6 (6.5)	4 (6.3)	75 (5.4)	4 (3.3)
Assistance and personal income	37 (39.8)	22 (34.9)	535 (38.6)	41 (34.2)
Only personal income	41 (44.1)	30 (47.6)	708 (51.1)	71 (59.2)
Missing	9 (9.7)	7 (11.1)	68 (4.9)	4 (3.3)
Prenatal payment, n (%)				
No insurance	7 (7.5)	5 (7.9)	50 (3.6)	8 (6.7)
Any public/private assistance	48 (51.6)	28 (44.4)	705 (50.9)	52 (43.3)
VA/commercial/HMO	38 (40.9)	30 (47.6)	630 (45.5)	60 (50.0)
Missing	0	0	1 (0.1)	0

Characteristic	Stillbirths		Livebirths	
	SCRN (n=93)	study (n=63)	SCRN (n=1386)	study (n=120)
Partnership status, n (%)				
Not cohabiting	22 (23.7)	14 (22.2)	263 (19.0)	19 (15.8)
Cohabiting and not married	21 (22.6)	13 (20.6)	324 (23.4)	28 (23.3)
Cohabiting and married	42 (45.2)	30 (47.6)	740 (53.4)	70 (58.3)
Missing	8 (8.6)	6 (9.5)	59 (4.3)	3 (2.5)

Abbreviations: BMI, body mass index; HMO, Health Maintenance Organization; SD, standard deviation; SLE, significant life events; UTHSC, University of Texas Health Sciences Center at San Antonio; UTMB, University of Texas Medical Branch at Galveston; VA, Veterans' Affairs.

[a] *Smoke exposure was yes if (a) mothers reported any smoking or tobacco use up to two years prior to maternal interview or (b) cotinine concentration in maternal blood samples taken at delivery exceeded the SCRN-designated threshold for passive or second-hand smoke exposure (0.25 ng/mL or more).*

[b] *Pregnancy complications was yes if any of 12 conditions had been noted in maternal charts as occurring during the delivery hospital visit (e.g,. premature rupture of membranes, preeclampsia). See Appendix B.*

[c] *Pre-existing maternal conditions was yes if medical records or maternal interviews recorded the pre-pregnancy presence of any of 23 conditions including diabetes and heart disease. See Appendix B.*

[d] *Maternal gestational conditions was yes if any of 29 conditions (e.g., diabetes, hypertension) had been recorded as present during pregnancy in maternal charts or maternal interview. See Appendix B.*

[e] *BMI was abstracted from charts and calculated from maternal pre-pregnancy weight.*

4.3.2 Associations between stressors and stillbirth

Disadvantage: In the study sample, having two or more Disadvantage items as compared to none yielded an OR of 4.53 (95% CI 1.58, 12.93), with a significant test for trend (p <0.005) (Table 9). Estimates in SCRN were slightly attenuated in comparison. Models using a continuous version of this exposure found that every additional item in Disadvantage was associated with 80% greater adjusted odds of stillbirth (Table A51). Sensitivity analyses excluding three pregnancies (two outliers and one that had multiple quality control flags) (n=180) and using a modified version of Disadvantage excluding partnership status yielded slightly stronger ORs (Table A52).

SLE: There was no evidence of an association between SLE and stillbirth in either the study sample (OR 1.54 for 4+ vs no Significant Life Events, 95% CI 0.55, 4.28) or SCRN (OR 1.17, 95% CI 0.58, 2.36) (Table 9). The test for trend in the study sample was not significant (p<0.4), and models using the continuous version of this exposure were consistent with these

results (Table A51), as was a sensitivity analysis in a restricted study sample (n=180) (Table A52). Due to these null findings, we proceeded with methylation association analyses for Disadvantage only.

Table 9: Odds ratios (95% CIs) relating stressors (SLE and Disadvantage) and stillbirth in the study sample (n=183) and SCRN (n=1,479)

	Study		SCRN	
	OR (95% CI)	**aOR [a] (95% CI)**	**OR (95% CI)**	**aOR [a] (95% CI)**
Disadvantage				
0 items	ref	ref	ref	ref
1 item	1.51 (0.74, 3.05)	1.65 (0.76, 3.56)	1.71 (1.05, 2.78)	2.06 (1.21, 3.51)
2+ items	2.96 (1.17, 7.70)	4.53 (1.58, 12.93)	1.83 (1.04, 3.23)	2.40 (1.29, 4.47)
SLE				
0 events	ref	ref	ref	ref
1 event	0.84 (0.33, 2.13)	1.15 (0.41, 3.17)	0.97 (0.49, 1.89)	0.97 (0.49, 1.93)
2 events	1.38 (0.52, 3.67)	1.71 (0.61, 4.83)	1.31 (0.68, 2.55)	1.32 (0.67, 2.60)
3 events	1.07 (0.32, 3.36)	1.20 (0.36, 4.05)	1.27 (0.59, 2.75)	1.24 (0.56, 2.73)
4+ events	1.62 (0.63, 4.20)	1.54 (0.55, 4.28)	1.43 (0.74, 2.79)	1.17 (0.58, 2.36)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; ref, reference level; SCRN, Stillbirth Collaborative Research Network; SLE, Significant Life Events.
[a] Adjusted for maternal age, site, and race. SLE aORs also adjusted for Disadvantage (measured continuously).

4.3.3 Associations between methylation, stressors and stillbirth

In **Step 1**, the initial analysis of associations between methylation of 1,191 CpGs, stressors and stillbirth identified 35 differentially methylated CpGs and six DMRs, all in relation to stillbirth (see Table A53 for CpGs and Table A54 for DMRs). In **Step 2**, further analysis identified 32 CpGs and six DMRs associated with stillbirth, and six CpGs associated with Disadvantage. See Table A55 for the Pearson correlation coefficients of the beta values of the constituent CpGs for each DMR. Six CpGs were associated with both stillbirth and Disadvantage; none of the DMRs were. In **Step 3**, we eliminated two CpGs for which associations with Disadvantage and stillbirth were in opposing directions. The remaining four CpGs were tested for evidence of mediation. See Figure 14 for a summary of how they were identified from the initial group of 1,191 CpGs.

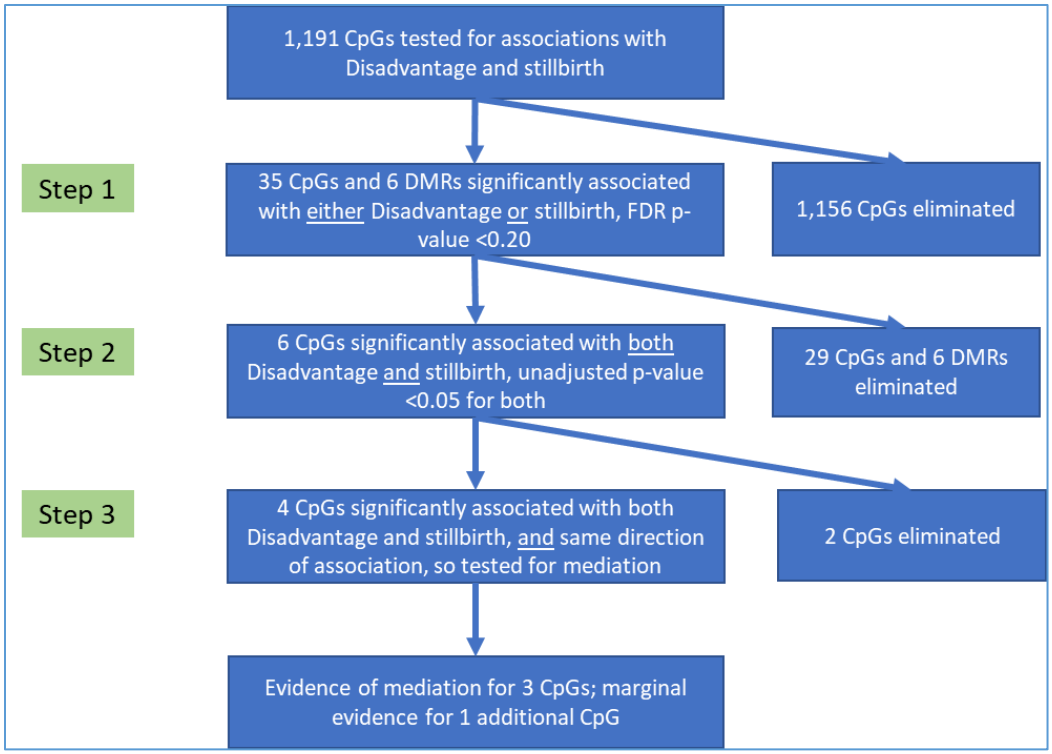

Figure 14: Flowchart showing how screening identified mediation candidates

Abbreviations: CpG, cytosine-guanine base pair; DMR, differentially methylated region; FDR, false discovery rate.

4.3.4 Mediation analyses

There was low correlation between the mediator candidates (Table A56). Methylation at three CpGs partially mediated associations between Disadvantage and stillbirth, including two on *IGF2* (cg02097792 and cg12283393) and one on *HSD11B2* (cg19413291), with *p*-values for the average causal mediation effect, ACME, less than 0.05, and *p*-values for the proportion of the effect mediated, PME, greater than 0.05, for the comparison of 2+ versus no Disadvantage items (Table 10). Models using the continuous version of Disadvantage showed that methylation of cg02097792 on *IGF2* mediated 21% of the association between Disadvantage and stillbirth (ACME *p*-value 0.012 and PME *p*-value 0.031); ACME *p*-values for the other CpGs were not significant (Table A57).

Table 10: Results of assessing evidence for whether methylation of 4 CpGs mediates associations between Disadvantage and stillbirth: Average causal mediation effect (ACME) *p*-values and average proportions of the effect mediated (PME) in 63 stillbirths and 120 livebirths

				Mediation effect [a]			Mean methylation beta values, SD (# births)	
ID	**Chr**	**Gene**		**ACME *P* [b]**	**PME**	**PME *P* [b]**	**Stillbirths**	**Livebirths**
cg02097792	11	*IGF2*	0 items				27.4, 2.4 (32)	26.1, 2.9 (79)
			1 item	0.110	31.3%	0.280	27.3, 3.6 (19)	26.3, 2.5 (31)
			2+ items	0.035	20.8%	0.067	27.1, 2.0 (12)	27.1, 2.2 (10)
cg12283393	11	*IGF2*	0 items				78.0, 7.1 (32)	82.7, 3.6 (79)
			1 item	0.880	-8.7%	1.000	77.5, 10.1 (19)	82.6, 2.7 (31)
			2+ items	0.044	17.2%	0.098	78.9, 2.8 (12)	81.1, 2.0 (10)
cg19413291	16	*HSD11B2*	0 items				79.2, 2.9 (32)	78.6, 2.9 (79)
			1 item	0.240	21.3%	0.470	80.0, 2.8 (19)	79.3, 2.6 (31)
			2+ items	0.048	24.0%	0.157	80.8, 2.3 (12)	79.5, 2.6 (10)
cg08362738	11	*BDNF*	0 items				3.8, 0.7 (32)	3.5, 0.7 (79)
			1 item	0.570	7.8%	0.610	3.8, 0.9 (19)	3.6, 0.7 (31)
			2+ items	0.105	15.2%	0.158	4.1, 0.6 (12)	3.6, 0.4 (10)

Abbreviations: ACME p, p-value for the average causal mediation effect; Chr, chromosome; CI, confidence interval; OR, odds ratio; PME p, p-value for the average proportion of the effect mediated; SD, standard deviation.
[a] Mediation models (one per CpG) used logistic regression and M values, and adjusted for site, maternal age, race, plate, cell type (trophoblast, stromal, endothelial, nRBC, and syncytiotrophoblast), and sex.
[b] p-values uncorrected.

4.4 Discussion

In a sample of 63 stillbirths and 120 livebirths, all full-term non-anomalous singletons, having two or more vs no items in an Index of Disadvantage was associated with more than quadrupled odds of stillbirth (95% CI 1.58, 12.93). We found no association between an Index of Significant Life Events and stillbirth, and hence did not proceed with mediation analyses using this exposure. We found that 32 out of 1,191 CpGs on five stress-related genes were differentially methylated with respect to stillbirth, and six CpGs were differentially methylated with respect to Disadvantage. Methylation at three CpGs (two on *IGF2* and one on *HSD11B2*) partially mediated associations between the Index of Disadvantage and stillbirth.

4.4.1 Interpretation of results

There is substantial evidence that maternal stress is associated with an increased risk of

adverse birth outcomes.[69 327] Recent studies have found, for example, associations between anxiety, depression, job stress and prenatal stress and adverse outcomes such as preterm birth and low birthweight.[328 329] However, few studies have examined associations between stress and stillbirth.[74 80] In Denmark, a study of 20,000 births found 90% increased odds of stillbirth in mothers with high vs intermediate stress as reported by mothers in a 12-item General Health Questionnaire,[78] and in Sweden, a study of 3 million births found that bereavement due to death of an older child was associated with doubled odds of stillbirth.[79] While these studies' populations and measures of stress differed from ours, the results are consistent with our finding of increased odds of stillbirth with greater stress as measured by an Index of Disadvantage. Our finding of no association between SLE and stillbirth was unexpected, diverging from Hogue et al. who found SLE and stillbirth to be associated in SCRN.[76] Differences may be due to our smaller sample size and to that study's inclusion of multiple, preterm, and anomalous births.

In seeking evidence for whether methylation may be a mechanism by which stress increases the risk of stillbirth, we found that three CpGs on two genes, *IGF2* and *HSD11B2*, may partially mediate associations between Disadvantage and stillbirth. We also found associations between methylation, stress and stillbirth for 35 CpGs on five genes, a result interesting in its own right. Below, we comment on our gene-specific findings, noting the proximity of significant CpGs to one another and to areas known to play functional roles in gene expression, as well as comparing our findings with the literature.

IGF2: *IGF2* is paternally expressed, meaning that the paternal allele is typically expressed while the maternal allele is "imprinted" or repressed. *IGF2*'s imprinting status is governed together with that of a paternally imprinted gene, *H19*, from a region upstream of the *IGF2* gene body called the imprinting control region (ICR). *IGF2* is involved in fetal and

placental development, and acts in concert with *H19* which is thought to help conserve allocation of maternal resources to the fetus.[330] Of the 334 CpGs that we analyzed on this gene, 16 were differentially methylated with respect to stillbirth, of which two were also differentially methylated with respect to Disadvantage. cg02097792, which mediated 21% of the association between Disadvantage and stillbirth, lies on an enhancer 92,000 bp upstream of the gene body and 37,000 bp downstream of the next closest significant CpG that we identified (which is in the ICR). The other CpG for which we found evidence of partial mediation, cg12283393, lies on a promoter at a transcription factor binding site (a region which governs the start of the transcription process, TFBS), and was also not near any other significant CpGs.

The remaining significant CpGs that we identified included a group of three on the gene body (cg01667319, cg10037494, and cg25163476) together with a DMR. Two of these CpGs lie on a CpG island (a type of genomic region defined by a high density of CpGs and for which methylation has been associated with repression of transcription), and two were in shore and shelf regions (shores are areas extending about 2,000 bp away from a CpG island on either side, and shelves extend an additional 2,000 bp in either direction).[331] A study of 39 CpGs covering a 9,000 bp region that starts just 305 bp downstream of this group found no association between methylation and birthweight.[287] However, that study's small sample size and use of principal components analysis to measure methylation could have obscured associations. The associations we found with stillbirth were, however, consistent with evidence from another study, which found that average methylation was inversely associated with placental weight and (marginally) birthweight, although that study focused on a region 6,000 bp upstream of this group of CpGs (rather distant).[294] We also found three groups of significant CpGs upstream of the *IGF2* gene body: (1) a group of four CpGs (cg14681632, cg10113191, cg19150916 and cg03776775) and a

DMR all within 2,830 bp of each other at a transcription factor binding site (TFBS) on a single promoter, with two CpGs on an island and two in shore/shelf regions; (2) a group of five CpGs (cg19290938, cg19290939, cg19290940, cg05894719 and cg03982897) and two DMRs located within 1,350 bp of one another in shore/shelf regions on an enhancer; and (3) one CpG, cg16574793, together with another DMR on a promoter in the imprinting control region (ICR) for *IGF2*.

Our results appear to be consistent with a small study that found an association between placental methylation in the imprinting control region of *IGF2* and stressful life events.[282] (Due to our null findings for SLE and stillbirth in our study sample, we did not explore associations with methylation for this exposure; nevertheless, the literature on SLE is still informative for our findings related to Disadvantage, insofar as we hypothesized that both are stressors.) *IGF2* mediators could contribute to repression of the paternal allele (Disadvantage was associated with hypermethylation of cg02097792) or expression of the maternal allele (Disadvantage was associated with hypomethylation of cg12283393), with adverse consequences for fetal growth, such as reduced placental size and capacity to nourish the fetus. However, the study referenced found no association between stress and *IGF2* expression, calling the functional relevance of methylation in this region into question, though small sample size may have been a factor in the null finding.

HSD11B2: *HSD11B2* encodes a protein responsible for converting cortisol to cortisone, protecting the developing fetus against maternal stress responses. *HSD11B2* has also been implicated in fetal growth. Of 322 CpGs examined, we found that 8 were differentially methylated with respect to stillbirth, of which three were also differentially methylated with respect to Disadvantage, including one, cg19413291, for which there was evidence suggestive of

partial mediation of associations between Disadvantage and stillbirth. This CpG lies downstream of the *HSD11B2* gene body in a shore region on a transcription factor binding site (TFBS) within 1500 bp of a transcription start site (TSS), an important region for gene function. It is on the same promoter as another CpG just 544 bp distant, cg00511334, which was also associated with stillbirth and lies on the 1st exon, another area implicated in gene function.[332] Another group of interest, 37,000 bp away from the partial mediator CpG and also downstream of the gene body, comprised two CpGs, cg05632351 and cg03498304. These CpGs, both associated with stillbirth, lie on a single promoter in the 5' UTR (untranslated region), another genomic region that is implicated in transcription. cg05632351 lies in a shore area and cg03498304 is on a CpG island; cg05632351 was also inversely associated with Disadvantage. Finally, cg01087710, upstream of the gene body on a promoter on a CpG island at least 73,000 bp distant from any other differentially methylated CpGs, was positively associated with stillbirth and inversely associated with Disadvantage. There is some evidence from the literature that is consistent with the inverse associations we found between Disadvantage and methylation at two CpGs (cg01087710 and cg05632351),[263] and with a mediating role of *HSD11B2* methylation for associations between stress and adverse pregnancy outcomes,[281] as well as evidence of associations between perceived stress and stressful life events and *HSD11B2* gene expression.[266 282] However, the CpGs included in these studies were all within or very close to (<150 bp) the *HSD11B2* gene body and at least 30,000 bp distant from the CpGs that we identified as significant.

BDNF: *BDNF* is a stress-related gene that plays a role in placental development. Of 144 CpGs examined, we found that four were differentially methylated with respect to stillbirth, of which one was also differentially methylated with respect to Disadvantage. These CpGs were located in two pairs. The first pair, on the gene body, included cg08362738 and cg04672351,

located within 250 bp of each other on a single promoter. One of these, cg08362738, was associated with both stillbirth and Disadvantage; it lies on a CpG island within 200 bp of a transcription start site (TSS). The other lies on a shore within 1500 bp of a TSS. Results from several studies found both positive associations (consistent with our results) and inverse associations (contrasting with our results) between stress and methylation in nearby regions, including in placental tissue.[279 290 304] Another study found inverse associations after allowing interaction between region type and stressor, an analysis we did not perform. Allowing interaction reversed the direction of association for CpGs on promoters and in shore and shelf regions.[305] An EWAS identified 26 additional CpGs on the gene body in the top 1-25% for associations between methylation and social deprivation or poor social environment, but we did not find any of these CpGs to be significant, possibly related to differences in stressors, tissue, these studies' use of mean rather than CpG-specific methylation, and our small sample.[304] The second pair of CpGs (cg27309677 and cg19372491) lay downstream of the gene body on one promoter, within 160 bp of each other, in the 5' UTR region, overlapping with a DMR, but in a region very distant from other CpGs reviewed in the literature (>385,000 bp).

FKBP5: *FKBP5* codes for the glucocorticoid receptor co-chaperone protein, helping to manage the stress response. Of 156 CpGs we examined, three were differentially methylated with respect to stillbirth. These included cg25026500 and cg25324046, both located on islands 200 bp from a transcription start site (TSS), and cg00065598, located 1500 bp from a TSS. These CpGs were at least 400,000 bp apart, with no other significant CpGs nearby. However, evidence from the literature is consistent with our results, and evidence of inverse associations between *FKBP5* methylation and gene expression is also consistent with a functional interpretation for methylation at these CpGs.[304 305]

NR3C1: *NR3C1* encodes the glucocorticoid receptor which plays a key role in stress response. Of 235 CpGs assessed, just one was differentially methylated with respect to stillbirth. A number of studies have found associations between *NR3C1* methylation and both stress[261 262 281 290 309] and adverse pregnancy outcomes.[311] Further, two studies found evidence consistent with *NR3C1* methylation as a mediator of associations between war stress and birthweight.[289 295] It was unexpected to have such sparse results in a gene strongly implicated in the stress response. Multiple differences across studies (for instance differences in exposures or outcomes, the use of average values or principal components rather than CpG-specific methylation, and our small sample size) may help to explain the contrast between our study and these results. Our null findings may also be due to unaccounted-for interaction; Appleton et al. found that hypermethylation of *NR3C1* interacted with hypomethylation of *HSD11B2* in associations with adverse newborn neurobehavior.[292]

4.4.2 Strengths and limitations

The observed associations could be causal, as associations between methylation, stress and stillbirth are biologically plausible. Stress processes are managed by the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-adrenal-medullary SAM axis, and our candidate genes play important roles in these axes. The HPA axis triggers a chain of events including the release of corticotropin-releasing hormone (CRH) and glucocorticoids such as cortisol, which act by binding to glucocorticoid receptors (GR). *NR3C1* encodes the GR and *FKPB5* encodes the GR co-chaperone protein. The SAM axis contributes to stress management by releasing catecholamines which help to increase blood flow and regulate the pulmonary and immune systems. Stress can overstimulate the HPA axis, and pregnancy increases levels of cortisol through the release of placental CRH. The fetus is normally protected against this extra

cortisol by the action of genes such as *HSD11B2*, but stress can imperil fetal health, in part by reducing *HSD11B2* expression.[333] Abnormal stress responses may also increase the expression of catecholamines, possibly decreasing blood flow to the placenta.[69 74 79 80 334 335] Consequences can include abnormal placental functioning, jeopardizing the delivery of oxygen and nutrients to the fetus, affecting fetal growth and contributing to other adverse fetal outcomes.[78 79 84-86 333 336 337] There is also evidence of links between stress and prenatal respiratory function in connection with *BDNF* methylation which may jeopardize fetal survival,[338] and between *IGF2* expression and fetal survival.[268 269]

However, much is unknown about the consequences of methylation for how genes actually function, raising questions about how to interpret our results. For example, methylation on gene bodies may increase rather than suppress expression, and methylation at transcription factor binding sites does not consistently repress expression,[319 339 340] while at CpG islands it may be more likely to.[331] Indeed, evidence of inverse associations between methylation and expression (hypermethylation "turning off" genes or hypomethylation "turning on" genes) was consistent with a functional interpretation for methylation of *HSD11B2* and *FKBP5* in relation to protein expression, but not for *IGF2*, calling into question the biological relevance of the *IGF2* mediators we identified. Moreover, other studies have shown that associations between methylation, stress and pregnancy outcomes vary by genotype and genomic region type, factors we were unable to account for, possibly driving a bias toward the null.[291 313] Also, lack of adjustment for confounders potentially important for the associations we studied may have inflated estimates; for instance, pollution levels could not be accounted for,[341] although frequency matching on site likely helped to address this factor.

To our knowledge, this was the first study to explore whether methylation is associated

with full-term stillbirth and mediates associations between stress and stillbirth. We used a nested case-control design, drawing stillbirths and livebirths from a larger multi-site population-based case-control study. Biosamples were extracted from placental tissue using standardized protocols. We analyzed all CpGs annotated to the microarray that were either on the gene body or on a promoter or enhancer for five candidate genes, in contrast to other candidate gene studies which often focus on a small number of previously-studied CpGs, often on the gene body. Methylation measures were CpG-specific and preserved direction of association. The study sample was limited to full-term non-anomalous livebirths and stillbirths, ensuring results were not due to preterm-related causes and making results less likely to be related to genetic factors. The consistency of our estimates for associations between SLE and stillbirth in the study sample and in the SCRN subset of full-term, non-anomalous, singleton births from which our study sample was drawn increases our confidence that selection bias was unlikely to have affected our results.

This study had several limitations. Data on perceived stress were unavailable, and if the selected indices do not actually measure maternal stress, our identified mediators would be mechanisms for a non-stress pathway. Indeed, some components of Disadvantage are associated with stillbirth directly; for instance, low income could postpone the start of prenatal care, increasing the possibility of pregnancy complications such as preeclampsia, resulting in stillbirth. By using Disadvantage as a proxy for stress, however, we hypothesized that these pathways were not only direct but also mediated by stress: low income increasing stress, concern over prenatal care increasing stress, and also pregnancy complications increasing stress. Exposures for stillbirth mothers were measured at a traumatic time in their lives, possibly leading to differential reporting of stressors between women with stillbirth and livebirth that could have inflated

estimates of associations between stress and stillbirth (recall bias). Cross-sectional data meant timing of exposures was unknown; SLE could have occurred up to three months prior to conception, or at any point during pregnancy. If the effect of stress is strongest during pregnancy, estimates may have been biased toward the null. However, our use of Disadvantage, which includes stressors likely established before conception and less vulnerable to recall bias (e.g., education), helped to mitigate the chances that these biases affected our estimates. Nonetheless, we could not discount the possibility of reverse causation, including through post-mortem changes in methylation, or if placental or fetal dysfunction leading to fetal death induced epigenetic changes while the fetus was still alive, thereby producing a spurious association between methylation and stillbirth.[342] Our analyses were necessarily limited by the number and location of CpGs annotated by the microarray, and our small sample size and use of unadjusted *p*-values for the final set of analyses may have introduced results that were due only to chance; however, the small number of comparisons (four for mediation analyses) made this less likely. The lack of gene expression data meant we could not be sure of the functional meaning of methylation in our study sample. Finally, the assumptions for causal mediation analysis, which include no unmeasured confounding of associations between stressors, methylation, and stillbirth, and no confounder of associations between methylation and stillbirth that is also on the pathway between stressors and stillbirth, may not have been met in our models.

4.4.3 Further study

Our results should be confirmed in a larger study that can assess correlations between methylation and gene expression to clarify the functional meaning of our mediation results. Models will need to allow for interaction between CpGs, as well as interaction with region types,[292 309] and should explore non-linear associations.[343] The DMRs we identified should be

further examined, with analyses accounting for within-individual correlation.[284 288 304 305 344-348] It would be ideal to also be able to ascertain the timing of stress exposures in a subsequent study. Our findings should be complemented by an epigenome-wide association study (EWAS) that allows investigation of additional stress pathways. Given evidence that methylation, stress, and stillbirth all vary with sex, sex-stratified analyses in a sufficiently large sample would help in learning more about this stress pathway for stillbirth.[268] We plan to use results from our primary models to inform further development of continuous versions of the exposure, such as the use of splines or quadratic terms, to better model the associations between stress, methylation and stillbirth. It will also be important to test the assumptions of mediation analyses. Finally, it proved challenging to identify which CpGs had been included in prior research. Researchers should routinely provide this data in a format that facilitates comparisons with the literature, identifying CpGs by their probe IDs and specifying genomic locations and the build used.[313]

4.4.4 Conclusion

Stillbirth is a tragedy that occurs in 26,000 families in the U.S. and nearly 2 million families globally each year. One-third of these deaths are unexplained. We provide evidence of associations between placental methylation of stress-related genes, hypothesized maternal stressors, and stillbirth, and of methylation of two stress-related genes as partial mediators of associations between stressors and stillbirth—a biological mechanism of effect. A logical question is how to reduce stress during pregnancy. One trial found that cognitive behavioral therapy in pregnancy significantly lowered perceived stress in treatment mothers,[349] and epigenetic changes themselves could potentially also be reversed, for instance through dietary supplements.[295 350] However, such interventions are impractical for the vast majority of mothers globally who are at higher risk of stillbirth, and more importantly, their focus on the individual

does not address the root causes of the deprivation-related stressors implicated in this study, such as low education and poverty. We hope that this study proves useful in making progress to improve our understanding of causes of stillbirth, as well as encouraging more researchers to include stillbirth as an adverse pregnancy outcome in studies of the effect of the epigenome on human health.

Chapter 5: Discussion and conclusion

5.1 Overview

The objective of this dissertation was to explore evidence that could help to explain persistent racial disparities in stillbirth. The specific aims were:

1. To review the literature on racial disparity in stillbirth rates;
2. To assess whether structural racism can help to explain racial disparity in stillbirth rates in NYC; and
3. To assess whether maternal stress is associated with stillbirth, whether stress is associated with methylation of stress-related genes, whether methylation is associated with stillbirth, and whether there is evidence that methylation of stress-related genes mediates associations between stress and stillbirth.

For **Aim 1**, we carried out a scoping review of the literature in five databases (PubMed, Scopus, Cinahl, Embase, PsycInfo) to identify all reports including stillbirth rates stratified by race in the U.S., mapping exposures and effect modifiers ("domains of analysis") and authors' comments on racial disparity in stillbirths ("domains of explanation") into one of eight domains (race, genetic, fetal, maternal, family, community, healthcare system, and structural). For **Aim 2**, we modelled associations between four measures of structural racism (Indices of Dissimilarity, Isolation, and Concentration at the Extremes, or ICE, and an Educational Inequity Ratio) and stillbirth in 546,983 non-Hispanic (NH) Black and white singleton births registered in New York City between 2009 and 2018, measuring exposures at the PUMA (Public Use Microdata Area) level. We tested for interaction between race and structural racism and estimated the odds of stillbirth separately in NH Black and NH white births for structural racism measures with evidence of interaction. For **Aim 3**, we assessed associations between maternal stressors (Indices

of Significant Life Events and Disadvantage) and stillbirth in 183 non-anomalous full-term singleton births (63 stillbirths and 120 livebirths) from the U.S. Stillbirth Collaborative Research Network. We then assessed whether maternal stressors and stillbirth were associated with differential methylation of 1,191 CpGs on five stress-related genes (*BDNF*, *FKBP5*, *HSD11B2*, *IGF2*, and *NR3C1)*, and whether methylation mediated associations between stressors and stillbirth.

In the first study, we found that the literature on racial disparities in stillbirth in the U.S. is characterized by a lack of investigation into health system and structural factors. In the second study, we found that structural racism as measured by ICE and Isolation was associated with stillbirth in NH Black but not NH white mothers; however, the associations were not in the expected direction. NH Black mothers living in PUMAs with a high concentration of privilege vs disadvantage had 90% *greater* odds of stillbirth (ICE quintile 5 vs 1), and NH Black mothers living in PUMAs that were the most vs least isolated had 40% *lower* odds of stillbirth (Isolation tertile 3 vs 1). While the measures may help to explain the Black-white disparity in stillbirth rates, our results raise questions about how they operationalize structural racism. We also found that in NH Black mothers, associations between ICE and stillbirth appeared to be stronger in older than younger women. This observation is consistent with the weathering hypothesis, including a possible stress pathway. The third study produced evidence of a mechanism by which such a pathway could increase the odds of stillbirth. We found that the association between the Index of Disadvantage and stillbirth was partially mediated by methylation of three CpGs on two stress-related genes, *IGF2* and *HSD11B2*.

5.2 Summary of results

5.2.1 Racial inequity in stillbirth rates constitutes a significant public health burden in the U.S.

We found a substantial literature related to racial disparity in stillbirth rates in the U.S. (Chapter 2), most of it fairly recent (50% of the 95 included reports were published after 2009). However, only 11 reports focused on racial disparity in stillbirth rates, with two-thirds including other outcomes. Chapters 2 and 3 revealed that the largest racial disparity in U.S. stillbirth rates is between Black and white births. We defined the Stillbirth Disparity Ratio (SDR) as the ratio of the stillbirth rate in a racial/ethnic minority group to the stillbirth rate in white births. We found 1,143 Black-white SDRs from 83 reports, with a median SDR of 1.67; 74% of these SDRs showed evidence of greater risk of stillbirth in Black than white births. Notably, although data were collected over a 70-year period (1945-2015), there was no indication of a change in SDR magnitudes over time. In NYC between 2009 and 2018 (Chapter 3), we found even greater disparity, with a nearly threefold greater risk of stillbirth in NH Black vs white births (13.8 vs 4.7 stillbirths per 1000 total births, respectively, yielding an SDR of 2.94). Data from NYC also showed a disparity in stillbirth rates among other racial/ethnic groups, with SBRs in Native American and Hispanic births of 7.7 and 6.2, respectively, as well as a very high SBR among mothers with unknown race (182.8 [sic] per 1000 total births) (Chapter 3). Our findings from Chapter 2 were inconsistent with these data, however, with less evidence of racial disparity for Native American and Hispanic births from our scoping review (median SDRs of 1.22 and 1.09, respectively). However, we also found that there was substantially less research attention to racial disparities for these groups, with just 42% and 14% of included reports providing relevant data for Native American and Hispanic births, respectively.

5.2.2 Individual-level risk factors are the main focus of research on disparities in stillbirth rates, but may not fully explain these disparities

In Chapter 2, we found that most research on racial disparities in stillbirth rates focuses on individual-level factors as domains of analysis (exposures or effect modifiers for regression analyses, stratification factors for risks). Nearly half of reports used fetal factors to analyze these disparities (46%) and over one-third used maternal factors (36%). The four most commonly-used categories of analysis among the 1143 Black-white SDRs were either fetal (gestational age, used by 41% of SDRs) or maternal (maternal age, prenatal care use (PNC), and education, used by 24%, 14%, and 13% of SDRs, respectively). (We defined PNC, e.g., number and timing of prenatal care visits, as a maternal characteristic, and quality of that care, e.g., barriers to access, as a health system characteristic.) The majority of SDRs in each of these categories showed evidence of disparity. This was true also when we looked at SDRs within subcategories. The top four categories of analysis used in Black-white SDRs show a 60-90% higher risk of stillbirth in Black vs white births regardless of the category being examined (median SDRs 1.62-1.89), with a 30% to twofold greater risk of stillbirth in every subcategory (median SDR ranges 1.30-1.85, 1.61-2.15, 1.47-1.98, and 1.73-2.06 for gestational age, maternal age, PNC, and education subcategories, respectively). This suggests that maternal and fetal factors fail to fully account for the observed racial disparities. The exception was a group of very preterm SDRs for which NH Black rates were lower than white rates (in alignment with Chapter 3 data indicating a Black-white SDR<1 for births at 20-27 weeks).

A logical possibility is that domains of analysis which have been under- or unexamined may be at least partly responsible for the disparity. Yet our scoping review demonstrated that family and community factors, healthcare system factors, and structural factors, though

commonly used as domains of explanation (20-38% of reports), were rarely (family/community, structural, 4-5%) or never (healthcare system) used as domains of analysis, with just seven of 95 reports examining either community- or structural-level factors.

5.2.3 Structural racism measures may help to explain Black-white disparity in stillbirth rates in NYC, but results were not in the expected direction

In Chapter 3, we selected four existing measures of structural racism from the extensive literature on structural racism and adverse pregnancy outcomes. We relied on the literature to guide us in our expectations for how these measures would be associated with stillbirth in Black and white mothers. The literature codifies high levels of disadvantage and high levels of isolation (as measured by ICE and the Index of Isolation, respectively) as indicative of higher structural racism. Since we hypothesized that structural racism can help to explain Black-white disparity in stillbirth rates, we therefore expected to find that residence in PUMAs with high levels of disadvantage and high levels of isolation would be associated with increased odds of stillbirth in NH Black mothers. Instead, we found the reverse. Among NH Black mothers, the odds of stillbirth were 90% *greater* with residence in PUMAs of privilege (ICE quintile 5 vs 1) and 40% *lower* with residence in highly isolated PUMAs (Isolation tertile 3 vs 1). Further, we found no evidence of associations between either of these exposures and stillbirth for NH white mothers. These results seem consistent with our hypothesis that structural racism may help to explain racial disparity in stillbirth rates, yet associations were not in the expected direction, and contrasted with much of the literature.

One possible explanation for our results was type I error (incorrectly rejecting the null hypothesis of no association between structural racism and stillbirth in NH Black births). However, the consistency of our findings for these two exposures, and the fact that our sample

size was large, suggests that the effects could be real rather than artefactual. Replication of our results in another large metropolitan area would lend support to our conclusions. Another possibility is that our model was incorrectly specified. Specifically, our choice to adjust for PUMA-level covariates for poverty level and proportion of Black residents may have introduced over-control, since these contributed to construction of both ICE and Isolation. However, when we adjusted only for individual-level covariates, we still found significant associations in the same direction in NH Black mothers, although for ICE they were attenuated. Finally, live birth bias might help to reconcile our results with the literature. Most studies of adverse pregnancy outcomes are likely to have excluded stillbirths, thereby conditioning on survival status, which can introduce live birth bias. A 2015 study of associations between prenatal exposure to PFAS and ADHD in school-aged children found that restricting the population to live births resulted in modest underestimates and even reversals of the direction of association depending on assumptions about the presence and strength of true associations between PFAS and ADHD, and about confounding of those associations.[241] A 2018 study found similar evidence for live birth bias in examination of associations between prescription drug use and pregnancy complications.[242] However, results from Williams et al., the only other study that has examined Isolation and stillbirth, and thus by definition not affected by live birth bias, also contrasted with our results.[64]

Another possibility is that the direction of association between structural racism and adverse pregnancy outcomes including stillbirth varies with the level at which structural racism is measured, such that structural racism manifests differently at different levels.[219 221] There is evidence of variation by level; for instance, data from Krieger et al. on associations between ICE and child mortality in NH Black families showed different directions depending on whether ICE

was measured at census tract level (increasing disadvantage conferred risk) or city level (estimates of association were non-significant but direction was reversed, suggestive of increasing privilege conferring risk).[219] If the associations we observed are not artefactual, the question remains as to whether and how they capture the effect of structural racism on stillbirth in NH Black women. While well-off, high-white-population neighborhoods may be enriched with health, education and other services that theoretically protect against stillbirth, these services may be less accessible or of lower quality for Black mothers.[235] Several studies have shown that Black women experience worse health outcomes regardless of access to healthcare, and receive lower quality of care than white women.[236 243-250] However, to explain our findings, subpar access to such resources would also need to render Black mothers in PUMAs of privilege worse off than Black mothers in PUMAs of disadvantage.

Another possible explanation lies in the concepts of 'privilege' and 'disadvantage', and the meaning of the measures we selected. Following the literature, we operationalized ICE such that low values were meant to represent disadvantage/higher levels of structural racism, and high values were meant to represent privilege/less structural racism. Therefore our results would suggest, perversely, that exposure to structural racism—as defined in the literature for these measures—is protective for NH Black mothers. However, structural racism *by definition* oppresses individuals due to their racial group membership, so such an interpretation does not make sense. Perhaps these measures represent a different underlying construct altogether. This would be challenging to reconcile with the extensive scholarship on structural racism, including 20 and 68 years of research using the ICE measure[216] and the Index of Isolation,[351] respectively; exploration of this possibility is beyond the scope of this dissertation.

Another possibility is that structural racism is manifesting as *low* Isolation (Isolation

tertile 1) and *high* ICE (ICE quintiles 4 and 5) when measured at the PUMA level (as opposed to, for instance, a lower level such as census tract or a higher level such as borough). Well-off white neighborhoods are populated predominantly by residents who are natively privileged due to their race, and hence may have fewer social supports for Black mothers and/or confer higher or more constant stress to NH Black mothers through a variety of pathways.[251] In contrast, residence in PUMAs with high concentrations of Black residents could, for example, reduce the frequency of interpersonal racist encounters and/or provide more social resources to reduce stress.[252] While our review of the literature on variations in direction and strength of estimates of association in relation to the level of measurement was inconclusive, it does suggest that structural racism manifests differently at different levels. The same racist processes that build segregated and inequitably resourced neighborhoods could also make residence in well-off white neighborhoods toxic (and residence in same-race neighborhoods relatively protective) for NH Black mothers. If so, this could help to make sense of our findings.

Our null results for Dissimilarity and Educational Inequity were also unexpected. In analyses in the total (Black + white) population, we found that residence in PUMAs with high Dissimilarity was associated with increased odds of stillbirth (OR 1.16 for tertile 3 vs 1), while for Educational Inequity, the association with stillbirth was not significant (OR 0.90 for tertile 3 vs 1); however, for neither exposure was there evidence of interaction with race. One explanation may be effect modification by degree of segregation. For instance, Brown et al. found that Black-white disparity in stillbirth rates was more pronounced in counties with high than low segregation.[81] Perhaps stratification by PUMA-level characteristics such as poverty might reveal variation in associations by race.

5.2.4 Patterns of stillbirth odds in non-Hispanic Black mothers in NYC appear to be consistent with predictions of the weathering hypothesis

We found several lines of evidence that appear to be consistent with the weathering hypothesis in racial disparity in stillbirth rates. First, results from Chapter 2 showed an increase in SDRs with greater maternal age among the 273 SDRs that used this as a category of analysis, from a median SDR of 1.61 in mothers aged <20 to a median SDR of 2.15 in mothers aged 35+, a more than doubled risk of stillbirth among Black vs white births in these older mothers. Second, Chapter 3 bivariate analyses showed that the highest risk maternal age category was <20 for NH white mothers but 35+ for NH Black mothers. Third, *a priori* hypotheses that racial disparity in stillbirth risk increases with maternal age appeared to be supported by our finding in Chapter 3 that associations between ICE and stillbirth were strongest in older NH Black mothers, with no evidence of associations in any age group in NH white mothers. These results contrasted with a recent study examining evidence for the weathering hypothesis in relation to stillbirth. Brisendine et al. found that racial disparity in stillbirth rates increased through age 34, but then declined.[153] However, they treated age as the exposure and did not investigate any other risk factors that might produce increased stress, such as our structural racism exposures. While there is evidence that structural racism itself is a stressor, nonetheless a key limitation of our analysis in regard to this hypothesis is lack of perceived stress data.[204 205 250] Other possible explanations for our results include greater resilience in younger Black mothers living in neighborhoods of privilege, or different meanings of 'privilege' and 'disadvantage' for younger vs older Black mothers.

5.2.5 Epigenetic modification is associated with both stillbirth and disadvantage-related stressors

Chapter 3 findings were possibly consistent with a stress pathway between structural racism and stillbirth—that older Black mothers accrue the impact of accumulated stress over a longer period than younger Black mothers, translating into greater risk of fetal compromise. In Chapter 4, we found associations between Disadvantage, which we hypothesized is a maternal stressor, and stillbirth, with the odds of stillbirth more than fourfold greater for mothers with 2+ vs no items in the Index of Disadvantage. However, we found no associations between Significant Life Events and stillbirth. One question is what mechanisms could support a stress pathway. Our scoping review identified only four reports that examined mechanisms for any type of racial disparity in stillbirth rates,[143-145 352] none of which looked at epigenetic mechanisms as mediators, nor any type of mediator for a stress pathway. In Chapter 4, we found that methylation of stress-related genes is associated with stillbirth, including 32 differentially methylated CpGs on all five candidate genes out of 1,191 CpGs assessed, and six differentially methylated regions (DMRs) (on *IGF2* and *BDNF*). We also found that Disadvantage and methylation are associated, with differential methylation at six CpGs (on *IGF2*, *BDNF*, and *HSD11B2*). It was surprising to find no association with methylation of *NR3C1* as this gene encodes the glucocorticoid receptor, a key component of the stress response. The null findings may be due in part to unaccounted-for interaction; Appleton et al. found that hypermethylation of *NR3C1* interacted with hypomethylation of *HSD11B2* in associations with adverse newborn neurobehavior.[292]

5.2.6 Methylation maybe one mechanism through which disadvantage-related stressors increase the odds of stillbirth

We found that Disadvantage is associated with increased odds of stillbirth in part through a pathway mediated by methylation of stress-related genes. Methylation at cg02097792 on *IGF2* mediated 21% of the association between Disadvantage and stillbirth (*p*-value for the average causal mediation effect, ACME, 0.012), with evidence for partial mediation by methylation at two additional CpGs, cg12283393 on *IGF2* and cg19413291 on *HSD11B2*. These results demonstrate that while Disadvantage likely is associated with stillbirth through multiple pathways, epigenetic modification of stress-related genes may be one mechanism of effect. Methylation may mediate only some of the pathways between Disadvantage and stillbirth, and this may vary depending on the gene. Taken together, our results suggest a role for the placental epigenome in translating maternal stress into increased odds of stillbirth.

5.3 Strengths and limitations

5.3.1 Strengths

The main strength of this dissertation was its focus on an under-researched area of major public health significance through examination of racial disparity in stillbirth rates at both ends of the 'causal spectrum', examining not only upstream causes but also mechanisms of effect. In Chapter 2, our search was comprehensive. We systematically extracted data to construct 1,143 Black-white SDRs, providing a large dataset in which to examine analytical approaches to racial disparity in stillbirth rates. In Chapter 3, we included all births in NYC over a 10-year period, with little room for selection bias to affect results, and assessed associations with stillbirth using four measures of structural racism covering three domains (segregation, poverty, and educational inequity) with multiple sensitivity analyses to assess the robustness of our findings. Our analytic

approach allowed us to examine differences in associations by race. In Chapter 4, our case-control study was nested within a population-based case-control study. We used two measures of maternal stressors and examined associations with methylation at all relevant CpGs on five genes known to be related to stress and/or adverse pregnancy outcomes, not only on gene bodies but also at other promoter and enhancer sites. Methylation measures were CpG-specific and taken from placental tissue. The study sample was limited to full-term non-anomalous births, ensuring that results were not due to preterm-related causes and making results less likely to be related to genetic factors.

5.3.2 Limitations

A key limitation of the dissertation was our lack of perceived stress data. In Chapter 3, this meant we were unable to assess whether associations between structural racism and stillbirth include a maternal stress pathway, although this was suggested by evidence consistent with the weathering hypothesis. In Chapter 4, the lack of perceived stress data meant we had to rely on hypothesized maternal stressors. Another limitation was our lack of gene expression data, meaning that we do not know whether our mediation results actually have a functional interpretation. For both Chapters 3 and 4, another limitation was our use of cross-sectional data. While in both cases, the nature of the exposures and outcomes meant that reverse causality was unlikely, knowing more specifically the timing and duration of the exposures would have added useful nuance to our interpretation of results. For example, for Chapter 3 this would mean an ability to explore whether length of residence in PUMAs of privilege or disadvantage modifies associations, and in Chapter 4 we could have delved into whether pregnancy, pre-pregnancy, or even childhood exposure matters for these associations. For Chapter 3, our models may have been mis-specified, for instance if adjusting for PUMA-level covariates resulted in over-control.

For Chapter 4, it was beyond the scope of this dissertation to investigate interactions between CpGs and with region types (see below under Further studies). Finally, another important limitation for Chapter 4 was the strong assumptions for causal mediation analysis, which may not have been met in our models.

5.4 Further studies

5.4.1 Further explore structural racism and stillbirth

Given the strong correlation between ICE and Isolation, the next step for our structural racism study will be to further examine whether and how these measures interact. Variations in results depending on the level of measurement must be explored to assess whether the unexpected direction of our associations with ICE and Isolation are indeed dependent on level, and whether measurement at "higher" (e.g. borough) and "lower" (e.g. census tract) levels produces results that are consistent with the literature. We will also further explore model specifications including modification rather than confounding by area-level characteristics such as poverty. Beyond these initial steps, we would also examine narrower age strata for evidence of weathering, and explore gestational age-specific analyses, since maternal stress may manifest differently in preterm and full term births; this is also suggested by our findings in Chapter 2 of a higher median SDR for early preterm than later gestational age births. Finally, subsequent work should include systematically reviewing the literature for research that has found or discussed similar directions of association for Isolation and ICE to those we found, and exploration of additional domains of structural racism, in particular justice and quality of healthcare, as no measures can fully represent this multidimensional construct.[353]

5.4.2 Further explore methylation as a possible mechanism of action for stillbirth

The next step for our methylation study will be to explore interaction between the CpGs we identified as partial mediators. We will also reexamine the candidate genes, representing the DMRs with principal components rather than mean methylation values and taking into account both within-individual correlation and possible interaction between genomic region types.[284 288 292 304 305 309 344-348] Another key follow-on study will be an agnostic epigenome-wide association study (EWAS), as it will allow investigation of additional stress pathways. Indeed, a more complete investigation of racial disparity in stillbirth rates would explore not only the epigenome but also other omics including the proteome and metabolomics, areas beyond the scope of this dissertation. It would also be useful to investigate whether age interacts with methylation, since a finding that mediation by methylation of stress-related genes is stronger in older than younger NH Black women would strengthen evidence for the existence of a stress pathway between structural racism and stillbirth in these women. Subsequent work should prioritize obtaining gene expression data. Evidence of correlation between increased gene expression (upregulation) and hypomethylation (or the reverse) would support a functional interpretation for methylation of the significant CpGs. It would also be of interest to repeat these analyses in preterm births, since as mentioned above, stress may work differently according to gestational age. For both Chapters 3 and 4, it would be very useful to obtain measures of perceived stress and assess directly the evidence for stress pathways for stillbirth. Finally, there has been little review of the effect of death on methylation and this merits further study.[354 355]

5.4.3 Carry out mixed methods research to contextualize findings

A major gap in this dissertation is the voices of the individuals affected by stillbirth, in particular NH Black mothers. Mixed methods research would be an important start in hearing

women's views on our research questions, the assumptions underlying our theoretical diagrams, the constructs measured by structural racism exposures such as privilege, our results, and our interpretation of our findings.[356] Women's insights and expertise would also be invaluable in suggesting new lines of inquiry, improving measures of structural racism, and contextualizing results.[357]

5.4.4 Explore the wider relevance of these results

A final area of further study is to examine the wider relevance of our results. This should start with an examination of the non-U.S. literature on racial/ethnic disparity in stillbirth rates. Exploring the relevance of our structural racism results could include repeating this study in other large metropolitan areas as well as potentially at a national level. A major gap identified by the scoping review was lack of research on race/ethnic groups other than Black. Native American and Hispanic mothers have higher stillbirth rates than white mothers, and these should be explored in relation to structural racism.

5.5 Conclusion

The objective of this dissertation was to explore evidence that could help to explain persistent racial disparities in stillbirth. Through Aim 1, we identified a key gap in the literature on racial disparity in stillbirth in the U.S., namely the lack of research on structural factors, and this provided the motivation for Aim 2. We found that structural racism as measured by ICE and Isolation was associated with stillbirth in NH Black but not NH white mothers. This would seem consistent with our hypothesis that structural racism may help to explain racial disparity in stillbirth rates, yet the associations were not in the expected direction. Our results raise questions about how these measures operationalize structural racism, meriting further investigation. We also found evidence that appears to be consistent with the weathering hypothesis. This provided

an additional motivation for Aim 3 which examines methylation as a biological mechanism that mediates associations between maternal stress and stillbirth.

Our research on methylation is mainly useful as an addition to the scientific literature on mechanisms of effect, as a generator of new hypotheses for further research. Given that approximately 30% of stillbirths are unexplained regardless of the extent of investigation; that most pregnancies with stillbirth risk factors (e.g., preeclampsia) still result in live birth; and that stillbirths considered "explained" may be ascribed to different causes depending on the classification approach, it is clear that some stillbirth causal factors remain to be identified. Maternal stress may be a "necessary but insufficient component cause", perhaps one hit in a multiple-hit model that tips the balance toward stillbirth in otherwise comparable pregnancies. This possibility is in line with similar hypotheses for increased risk of preterm birth with greater allostatic load.[358] Further, given that placental dysfunction and disorders may be responsible for a large proportion of "unexplained" stillbirths, stress may contribute to stillbirth by speeding up the process of placental ageing.[101 359 360] Ultimately, in women exposed to multiple stressors or stressors over time (e.g., weathering), and where Black women are living in a society permeated by structural racism, epigenetic modification could adversely affect placental capacity to protect and nourish the baby, weakening fetal capacity to withstand other blows, and tipping the balance toward stillbirth.[268]

Our finding that maternal stressors and structural racism are associated with stillbirth provides additional motivation for health providers to work with individuals to identify sources and levels of stress in their lives and collaborate with mothers to try methods of stress reduction. (These would potentially include peer support groups, meditation, mindfulness, and so on, if policies and programs are put in place and funded.) Yet, while stress reduction techniques can

certainly be useful,[361 362] focusing on such interventions inadvertently reinforces a culture of blaming mothers for stillbirth rather than looking to upstream causes of stress, and removing these.

A recent paper in the *New England Journal of Medicine* reviewing structural racism as a fundamental cause of health inequities in the U.S. argues that only dismantling structural racism can ultimately remove the downstream effects, such as the racial disparity in stillbirth rates explored in this dissertation.[353] A large literature describes the multitude of actions that can be taken to dismantle structural racism.[63 363] There are also numerous reports that highlight how stillbirths can be prevented globally and in the U.S. Many of these actions overlap, and it is in this overlap where actions to sustainably reduce racial disparity in stillbirth rates in the U.S. may be found. See Figure 15, which summarizes some of these actions.[7 353]

Research on causes is a critical component of stillbirth prevention and reducing the inequitable distribution of this public health burden. Limited understanding of causes at both "ends of the spectrum", from upstream distal factors to mechanisms, has likely contributed to slow progress on prevention.[7 8] This dissertation contributes to science and public health by providing researchers with data to support new lines of inquiry, e.g., into associations between structural racism and stillbirth, and for methylation as a mechanism of association, that may help to improve our understanding of causes. It may also support health policy makers who now have additional data to illustrate the adverse health outcomes of structural racism in the U.S. Finally, it may help the parents and other family members of stillborn babies who continually seek to understand "why".

1. Document the health impact of structural racism and other upstream causes of inequities in stillbirth rates, e.g.,
   - increase researcher attention to and donor funding for these inequities and structural causes
   - develop tracking tools together with women and civil society groups
   - put useable data into the hands of the people affected
2. Improve the quality and quantity of data for structural racism and stillbirth, e.g.,
   - develop better measures of structural racism
   - develop consumer-driven measures of and data on quality healthcare
   - enable better data on stillbirths and stillbirth disparity in the U.S.
3. Dismantle structural racism within the public health community, e.g.,
   - increase access to respectful care, including policies and programs to retrain caregivers to decrease bias
   - reframe maternal and newborn/stillbirth care as a human rights/reproductive justice issue, including ensuring equitable access to quality healthcare before, during and after pregnancy and birth
   - develop new, culturally acceptable models of pregnancy care
   - work to ensure access to the new models through better insurance coverage
4. Support social action and cultural change, e.g.,
   - listen to women and recognize them as experts in what quality, equitable, respectful care means
   - provide platforms for women to engage directly with researchers, clinicians, policy makers, educators and donors as partners in research and healthcare

Figure 15: Interventions to reduce Black-white racial disparity in stillbirth rates[7 27 102 364-366]

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Appendix A: Additional tables and figures

Additional tables and figures for Chapter 2

Table A1: Search strategy

PubMed		Scopus		Cinahl		Embase		PsycInfo	
notes	**string**	**notes**	**string**	**notes**	**string**	**Notes**	**string**	**notes**	**string**
Limits									
• English • Title and abstract (automatically also includes author keywords) • Explodes all by default • Do not search for articles that feature the MeSH term as a Major Topic with [Majr], or restrict the MeSH term with one or more relevant subheading(s)		• LANGUAGE(english) • TITLE-ABS-KEY, which includes keywords also • No thesaurus		• English language • Title, Abstract and Subject headings is the default so no need to specify • Explode all • Do NOT need to include the 'narrower' terms (but ok to) • Do NOT select 'major concepts'		• English • Title, abstract and keywords for free text terms (keywords) only: .ti,ab,kw. and do not check "map to preferred term" • For EMTREE terms, check: o "map to preferred term in EMTREE" (/de) o "explode using narrower EMTREE terms" (/exp)		• English language • AB OR TI for abstract and title • Explode manually • Default "apply equivalent subjects" is ok	
Synonyms for RACIAL DISPARITY (thesaurus only)									
Thesaurus terms									
	"health status disparities"	n/a (no thesaurus and covered by free text)		CINAHL subject heading	"Health Status Disparities"	Preferred term is "health disparity"	"health disparity"	Use "health disparities"; also "racial disparities" and "equity", "racial and ethnic differences"	"health disparities"
Checked from PsycInfo but this is included within "race factors" MeSH term		n/a (no thesaurus and covered by free text)		Checked from PsycInfo but included in Race Factors and Health status disparities		Not an EMTREE term			"racial disparities"
Added from Cinahl	"race factors"	n/a (no thesaurus and covered by free text)			"Race Factors"	Preferred term is "race", already included		Not in thesaurus	
Checked from PsycInfo but		n/a (no thesaurus and		Checked from PyscInfo but		Not an EMTREE term			"racial and ethnic differences"

PubMed		Scopus		Cinahl		Embase		PsycInfo	
notes	**string**	**notes**	**string**	**notes**	**string**	**Notes**	**string**	**notes**	**string**
not a MeSH term		covered by free text)		included in Race factors and Ethnic groups					
Synonyms for RACE (thesaurus and free text)									
Thesaurus terms									
Not a MeSH term		n/a (no thesaurus and covered by free text)		Not a CINAHL subject heading; can use “Ethnic Groups” which includes these; also “Race Factors”			“race”		“Race (anthropological)”
Added from Cinahl	“minority groups”	n/a (no thesaurus and added new term so that it is covered by free text)			“Minority Groups”	Included under “population group” which will be exploded			“minority groups”
Added from Cinahl	“ethnic groups”	n/a (no thesaurus and covered by free text)			“Ethnic Groups”	Preferred terms are “ethnic group” and “population group”	“ethnic group”	Term is “racial and ethnic groups”	“racial and ethnic groups”
Added from Embase	“population groups”	n/a (not covered by free text since either word would be way too general)		Checked from Embase but included in Minority groups			“population group”	Not in thesaurus	
Free text terms									
	race		race		race		race		race
	racial		racial		racial		racial		racial
	ethnic*		ethnic*		ethnic*		ethnic*		ethnic*
	minorit*		minorit*		minorit*		minorit*		minorit*
Synonyms for DISPARITY (thesaurus and free text)									
Thesaurus terms									
Not a MeSH term		n/a (no thesaurus and covered by free text)		Delete (not in thesaurus)		This is a ‘candidate term’ in Embase	“disparity”	Not in thesaurus	
Checked from PsycInfo but not a MeSH term		n/a (no thesaurus and added new term so that it		Checked from PsycInfo but not in thesaurus		This is a ‘candidate term’ in Embase	“equity”		“equity”

PubMed		Scopus		Cinahl		Embase		PsycInfo	
notes	**string**	**notes**	**string**	**notes**	**string**	**Notes**	**string**	**notes**	**string**
		is covered by free text)							
Free text terms									
	disparit*		disparit*		disparit*		disparit*		disparit*
	inequit*		inequit*		inequit*		inequit*		inequit*
	equity		equity		equity		equity		equity
Synonyms for STILLBIRTH (thesaurus and free text)									
Thesaurus terms									
	"stillbirth"	n/a (no thesaurus and covered by free text)		'perinatal death' and 'pregnancy outcome' suggested as other CINAHL subject headings	"stillbirth"		"stillbirth"	Not in PsycInfo thesaurus	
	"fetal death"	n/a (no thesaurus and covered by free text)		Delete (not in thesaurus)		Preferred term is "fetus death"	"fetus death"	Not in PsycInfo thesaurus	
Added from Cinahl	"perinatal death"	n/a (no thesaurus and covered by free text)			"perinatal death"		"perinatal death"	Not in PsycInfo thesaurus	
	"perinatal mortality"	n/a (no thesaurus and covered by free text)					"perinatal mortality"	Not in PsycInfo thesaurus	
	"pregnancy outcome"	n/a (not covered by free text since either word would be way too general)		In thesaurus	"Pregnancy outcome"	This is a 'candidate term' in Embase	"Pregnancy outcomes"	Not in PsycInfo thesaurus	
Free text terms									
	stillb*		stillb*		stillb*		stillb*		stillb*
	still-b*		still-b*		still-b*		still-b*		still-b*
	"still born"		"still born"		"still born"		"still born"		"still born"
	"still borns"		"still borns"		"still borns"		"still borns"		"still borns"
	"still birth"		"still birth"		"still birth"		"still birth"		"still birth"
	"still births"		"still births"		"still births"		"still births"		"still births"
	deadborn		deadborn		deadborn		deadborn		deadborn
	"spontaneous termination"		"spontaneous termination"		"spontaneous termination"		"spontaneous termination"		"spontaneous termination"
	"spontaneous terminations"		"spontaneous terminations"		"spontaneous terminations"		"spontaneous terminations"		"spontaneous terminations"

PubMed		Scopus		Cinahl		Embase		PsycInfo	
notes	**string**	**notes**	**string**	**notes**	**string**	**Notes**	**string**	**notes**	**string**
Synonyms for DEATH (free text only)									
	death*		death*		death*		death*		death*
	dead		dead		dead		dead		dead
	mortal*		mortal*		mortal*		mortal*		mortal*
	wast*		wast*		wast*		wast*		wast*
	loss*		loss*		loss*		loss*		loss*
	demise		demise		demise		demise		demise
Synonyms for FETAL (free text only)									
	antepartum		antepartum		antepartum		antepartum		antepartum
	ante-partum		ante-partum		ante-partum		ante-partum		ante-partum
	“ante partum”		“ante partum”		“ante partum”		“ante partum”		“ante partum”
	intrapartum		intrapartum		intrapartum		intrapartum		intrapartum
	intra-partum		intra-partum		intra-partum		intra-partum		intra-partum
	“intra partum”		“intra partum”		“intra partum”		“intra partum”		“intra partum”
	fetal		fetal		fetal		fetal		fetal
	foetal		foetal		foetal		foetal		foetal
	perinatal		perinatal		perinatal		perinatal		perinatal

Table A2: Definitions of domains used to categorize analysis and explanations for racial disparity in stillbirth rates

	Domain	Category	What the category included (NOTE: paraphrased from included reports)
Race	**Race**	**Race**	*By design, all reports conceptualized race as either an exposure or an effect modifier, or disaggregated stillbirth rates by race. For domains of analysis, we noted when race was conceptualized as an exposure. For domains of explanation, race included: different susceptibility threshold to stillbirth due to fetal race; Hispanic paradox; race of both parents*
Individual level domains	**Genetic**	**Genetic**	*possible genetic explanation, re timing of birth, maternal and paternal genetics; possible epigenetic and other biologic explanation; weathering (premature aging related to changes in physiology and biologic functioning brought about by prolonged high levels of stress); related to prior C-section; biological risk and protective factors accumulating over the lifecourse*
	Maternal	**Age**	*teenaged parents, older age, age at first pregnancy*
		Education	*low education, college education*
		Marital status	
		Weight	*obesity, overweight, height and weight, maternal birthweight, severe obesity; obesity-related morbidities; underweight*
		Stress	*history of trauma/adverse events, prolonged high levels of stress; chronic stress from discrimination and segregation, prenatal stress; allostatic load from racism; psychosocial stress; psychological risk and protective factors accumulating over the lifecourse; childhood exposure to stress, poverty; stigma with mixed race; behavioral, emotional, and cognitive responses to racial discrimination; patient attitude/bias*
		Nativity	*maternal characteristics which may be related to immigrant status*
		General health	*physical and mental health, differences in illness severity, preconception health, "maternal physiological situations", preconception health, healthy worker effect, healthy immigrant effect; disability: intersection between race and disability, intellectual and developmental disabilities*
		Maternal conditions	*diabetes, infections, perinatal history, medication use, hypertensive disorders/high blood pressure, convulsive disorders; different prevalence and severity/mortality from cardiovascular disorders (congestive heart failure, coronary artery disease, hypertension, stroke); comorbidities that may be risk factors for preeclampsia/eclampsia, including hypertension, diabetes, obesity, acute renal failure and chronic renal failure; anemia, chronic conditions, renal disease*
		Pregnancy-related conditions	*difference in type or severity; complications; gestational diabetes, preeclampsia; antepartum/intrapartum/obstetric complications of pregnancy, genital infections in pregnancy, maternal hypertension, premature rupture of membranes, placental abruption, placenta previa, bleeding, fever, cord/placenta/membrane complications, chorioamnionitis, hydramnios; low or high risk pregnancy generally; also treatment (for randomized controlled trials)*
		Prior adverse pregnancy outcomes	*prior C-section; prior loss, small for gestational age, preterm birth*
		Health insurance	*medical insurance status, public insurance, Medicaid coverage; military status: interaction with health insurance status*
		Prenatal care	*number of prenatal care visits, whether prenatal care initiated in trimester 1; no prenatal care, whether prenatal care was sought; use of prenatal care; preference for lower quality hospitals; utilization of healthcare*
		Knowledge, attitudes and practice re pregnancy	*patient demand for C-section, healthcare literacy, knowledge of the system; in vitro fertilization; prenatal attitude toward pregnancy, compliance with accepted medical standards, patient attitudes/bias/behaviors*

	Domain	Category	What the category included (NOTE: paraphrased from included reports)
		Other health-related behaviors	*"SES behaviors", health behaviors (nutrition/diet, healthy traditional diet, sleep, exercise, smoking), prenatal health behaviors*
	Fetal	**Gestational age**	*spontaneous preterm birth, full-term, shifting risk with race through gestational age range; post-term; antepartum/intrapartum*
		Birthweight	*low birthweight, "smaller" babies*
		Small for gestational age	*higher risk of small for gestational age in white preterm; intrauterine growth restriction, fetal growth restriction, <5th etc. centile, slow fetal maturation*
		Causes of death	*hydrops, congenital anomalies, severity of cardiac injury, maternal complications of pregnancy, maternal conditions unrelated to pregnancy, infant of a diabetic mother, placental dysfunction, unknown cause, fetal distress, intrauterine hypoxia and birth asphyxia, other respiratory conditions of fetus, other and ill-defined conditions originating in perinatal period*
		Parity	*also interpregnancy interval*
		Plurality	*multiples; Hispanic paradox may not hold for triplets*
		Sex	
		Year of birth	*also period (range of years)*
Group level domains	**Family**	**Families**	*childcare burden, teen fathers, family support, parent involvement, family structure and stability*
		Socioeconomic status	*income, socioeconomic status*
	Community	**Community**	*sociocultural protection in new immigrants, social and economic resources; different levels of social support; norm of selfless devotion to the maternal role (marianismo); social support; racial group identification; acculturation; also neighborhood quality; stressful environments due to high crime, limited political power and limited access to resources; social disorganization; physical and socio-economic environment; absent recreational space and leisure time facilities; unsanitary conditions; overcrowding; lack of shopping facilities and merchandise, food choices; actual maternal residence: specific city or location where baby was born, whether metropolitan or not, registration region*
System level domains	**Health system**	**Healthcare quality**	*receive lower quality, dissatisfaction with services, differences in clinical management, adequacy of prenatal care, differential benefit from medical advances; undiagnosed risk factors; active and successful management of small for gestational age; condition-specific prenatal care according to the underlying high-risk condition; undetected causes of fetal death e.g., diabetes, hypoxia, placental abruption; lack of uniformity in clinical management; content of care; assessment and earlier treatment of maternal disease; overcrowded facilities/overworked staff; institutional factors related to C-section*
		Healthcare access	*barriers: no local services, no transportation, high cost services, language barriers, access to specialized care; access to tertiary care hospitals/high-risk obstetrical care; Medicaid policy and policies for health support services e.g., transportation; policies for covering enabling services such as transportation, social work, and behavioral health; systems of care*
		Health interventions	*induction of labor; ultrasonography, amniocentesis, and tocolytics; medical treatment of certain risk factors (e.g., blood pressure, cholesterol, glycosylated hemoglobin); more aggressive treatment of hypertension; control of preexisting diseases before conception; more advanced interventions, such as the use of steroids, surfactant, and intrapartum antibiotics; inequity of the distribution of the intervention; access to other forms of obstetrical care for high-risk patients by limiting the number of ultrasound procedures per pregnancy, or limiting payment rates for specialty care (perinatology or maternal-fetal medicine), or restricting access to progesterone injections to prevent preterm birth*

	Domain	Category	What the category included (NOTE: paraphrased from included reports)
		Physicians	*physician behavior and bias; different treatment plans or recommendations; physician behavior re C-section, provider attitude, bias or behavior; low reimbursement rates and delays or ‘‘hassle-factor’’ in billing and payment process may lead to fewer physicians accepting Medicaid patients; low awareness of race and disability specific risks*
	Structural	**Racism**	*racism, structural racism, racial discrimination, (residential) segregation, systematic bias, stigma related to race, physical and socio-economic environment of segregated neighborhoods (lack of affordable housing, food choices), institutional bias; levels of and changes in segregation; higher cost, substandard housing; housing discrimination*
		Poverty	*cutbacks in federal poverty programs, percentage of the population living below the poverty level, and percentage of the population that is unemployed; spiraling effect of poverty, area-level poverty*
		Other structural factors	*(society-level, state-level) sociodemographic, societal, cultural, economic factors, socioecological, multisystem issues, general environmental stress/factors/effects, general social determinants of disparities, general socioeconomic factors, "poor demographics", social environment, differential benefit from social advances, sociopolitical context; sociopolitical determinants of poor health outcomes including persistent environmental stress; aspects of society that uphold structural racism; environmental risk and protective factors accumulating over the life course; multifactorial and interactive, limited access to social and economic resources; pollution (e.g., ozone); racial/ethnic composition of the state (separate from racism) or of the health area*

Table A3: Search results: EMBASE

Limits	Hits on 2-20-21
• English • Title, abstract and keywords for free text terms (keywords) only: .ti,ab,kw. and do not check "map to preferred term" • For EMTREE terms, check: o "map to preferred term in EMTREE" (/de) o "explode using narrower EMTREE terms" (/exp)	English limit applied for the below hits
Synonyms for RACIAL DISPARITY (thesaurus only)	
Thesaurus terms	• "map to preferred term in EMTREE" (/de) • "explode using narrower EMTREE terms" (/exp)
"health disparity"	21,593
Combine racial disparity terms with OR	n/a, just 1 term
Synonyms for RACE (thesaurus and free text)	
Thesaurus terms	• "map to preferred term in EMTREE" (/de) • "explode using narrower EMTREE terms" (/exp)
"race"	59,480
"ethnic group"	182,152
"population group"	1,047,843
Free text terms	.ti,ab,kw. and do not check "map to preferred term"
race	171,201
racial	57,507
ethnic*	109,553
minorit*	96,792
Combine race terms with OR	1,262,406
Synonyms for DISPARITY (thesaurus and free text)	
Thesaurus terms	• "map to preferred term in EMTREE" (/de) • "explode using narrower EMTREE terms" (/exp)
"disparity"	11
"equity"	28
Free text terms	.ti,ab,kw. and do not check "map to preferred term"
disparit*	96,900
inequit*	12,961
equity	19,818
Combine disparity terms with OR	122,244
Combine race and disparity terms with AND	50,646
Combine race/disparity and racial disparity terms with OR	63,673
Synonyms for STILLBIRTH (thesaurus and free text)	
Thesaurus terms	• "map to preferred term in EMTREE" (/de) • "explode using narrower EMTREE terms" (/exp)
"stillbirth"	17,835
"fetus death"	38,475
"perinatal death"	3,911
"perinatal mortality"	23,181
"Pregnancy outcomes"	59,165
Free text terms	.ti,ab,kw. and do not check "map to preferred term"
stillb*	19,718

Limits	Hits on 2-20-21
still-b*	23,107
“still born”	219
“still borns”	16
“still birth”	810
“still births”	523
deadborn	1
“spontaneous termination”	240
“spontaneous terminations”	18
Combine stillbirth terms with OR	139,351
Synonyms for DEATH (free text only)	.ti,ab,kw. and do not check “map to preferred term”
death*	1,149,873
dead	68,149
mortal*	1,107,173
wast*	207,429
loss*	1,273,656
demise	9,659
Combine death terms with OR	3,376,779
Synonyms for FETAL (free text only)	.ti,ab,kw. and do not check “map to preferred term”
antepartum	7,943
‘ante-partum’	451
“ante partum”	451
intrapartum	11,862
‘intra-partum’	510
“intra partum”	510
fetal	294,151
foetal	21,205
perinatal	90,691
Combine fetal terms with OR	391,157
Combine fetal and death with AND	83,275
Combine fetal death and stillbirth with OR	190,840
Combine fetal death/stillbirth and racial disparity/race/disparity with AND	1,193
Issues noted	Fine; got both Brown and Williams

Search query

(('health disparity'/exp AND [english]/lim) OR ((('race'/exp AND [english]/lim) OR ('ethnic group'/exp AND [english]/lim) OR ('population group'/exp AND [english]/lim) OR (race:ab,kw,ti AND [english]/lim) OR (racial:ab,kw,ti AND [english]/lim) OR (ethnic:ab,kw,ti AND [english]/lim) OR (minorit*:ab,kw,ti AND [english]/lim)) AND (('disparity'/exp AND [english]/lim) OR ('equity'/exp AND [english]/lim) OR (disparit*:ab,kw,ti AND [english]/lim) OR (inequit*:ab,kw,ti AND [english]/lim) OR (equity:ab,kw,ti AND [english]/lim)))) AND ((('stillbirth'/exp AND [english]/lim) OR ('fetus death'/exp AND [english]/lim) OR ('perinatal death'/exp AND [english]/lim) OR ('perinatal mortality'/exp AND [english]/lim) OR ('pregnancy outcome'/exp AND [english]/lim) OR (stillb*:ab,kw,ti AND [english]/lim) OR ('still-b*':ab,kw,ti AND [english]/lim) OR ('still born':ab,kw,ti AND [english]/lim) OR ('still borns':ab,kw,ti AND [english]/lim) OR ('still birth':ab,kw,ti AND [english]/lim) OR ('still births':ab,kw,ti AND [english]/lim) OR (deadborn:ab,kw,ti AND [english]/lim) OR ('spontaneous termination':ab,kw,ti AND [english]/lim) OR ('spontaneous terminations':ab,kw,ti AND [english]/lim)) OR (((death*:ab,kw,ti AND [english]/lim) OR (dead:ab,kw,ti AND [english]/lim) OR (mortal*:ab,kw,ti AND [english]/lim) OR (wast*:ab,kw,ti AND [english]/lim) OR (loss*:ab,kw,ti AND [english]/lim) OR (demise:ab,kw,ti AND [english]/lim)) AND ((antepartum:ab,kw,ti AND [english]/lim) OR ('ante-partum':ab,kw,ti AND [english]/lim) OR ('ante partum':ab,kw,ti AND [english]/lim) OR (intrapartum:ab,kw,ti AND [english]/lim) OR ('intra-partum':ab,kw,ti AND [english]/lim) OR ('intra partum':ab,kw,ti AND [english]/lim) OR (fetal:ab,kw,ti AND [english]/lim) OR (foetal:ab,kw,ti AND [english]/lim) OR (perinatal:ab,kw,ti AND [english]/lim))))

Mapped terms

- 'health disparity' *mapped to* 'health disparity', *term is exploded*
- 'race' *mapped to* 'race', *term is exploded*
- 'ethnic group' *mapped to* 'ethnic group', *term is exploded*
- 'population group' *mapped to* 'population group', *term is exploded*
- 'disparity' *mapped to* 'disparity', *term is exploded*
- 'equity' *mapped to* 'equity', *term is exploded*

Limits	Hits on 2-20-21
• 'stillbirth' *mapped to* 'stillbirth', *term is exploded* • 'fetus death' *mapped to* 'fetus death', *term is exploded* • 'perinatal death' *mapped to* 'perinatal death', *term is exploded* • 'perinatal mortality' *mapped to* 'perinatal mortality', *term is exploded* • 'pregnancy outcome' *mapped to* 'pregnancy outcome', *term is exploded*	

Table A4: Search results: PubMed

Limits	Hits on 2-20-21
• English • Title and abstract (automatically also includes author keywords) • Explodes all by default • Do not search for articles that feature the MeSH term as a Major Topic with [Majr], or restrict the MeSH term with one or more relevant subheading(s)	English applied for the below hits
Synonyms for RACIAL DISPARITY (thesaurus and free text)	
Thesaurus terms	MeSH
"health status disparities"	16,299
“race factors”	365
Combine racial disparity terms with OR	16,606
Synonyms for RACE (thesaurus and free text)	
Thesaurus terms	MeSH
“minority groups”	14,124
“ethnic groups”	148,509
“population groups”	287,954
Free text terms	title/abstract
race	110,716
racial	43,607
ethnic*	146,928
minorit*	72,077
Combine race terms with OR	490,647
Synonyms for DISPARITY (thesaurus and free text)	
Thesaurus terms	MeSH
[none]	
Free text terms	title/abstract
disparit*	72,889
inequit*	11,328
equity	17,151
Combine disparity terms with OR	94,835
Combine race and disparity terms with AND	33,233
Combine race/disparity and racial disparity terms with OR	44,888
Synonyms for STILLBIRTH (thesaurus and free text)	
Thesaurus terms	MeSH
"stillbirth”	4,535
"fetal death"	23,501
“perinatal death”	1,183
“perinatal mortality”	2,656
"pregnancy outcome"	65,231
Free text terms	title/abstract
stillb*	14,613
still-b*	2,180
“still born”	166
“still borns”	6
“still birth”	380
“still births”	326
deadborn	5
“spontaneous termination”	161
“spontaneous terminations”	12
Combine stillbirth terms with OR	90,689
Synonyms for DEATH (free text only)	title/abstract
death*	804,078
dead	51,396
mortal*	744,011
wast*	148,512
loss*	957,447

Limits	Hits on 2-20-21
demise	6,623
Combine death terms with OR	2,424,031
Synonyms for FETAL (free text only)	title/abstract
antepartum	5,853
ante-partum	333
“ante partum”	333
intrapartum	8,852
intra-partum	296
“intra partum”	296
fetal	224,847
foetal	16,897
perinatal	66,555
Combine fetal terms with OR	298,858
Combine fetal and death with AND	58,549
Combine fetal death and stillbirth with OR	129,259
Combine fetal death/stillbirth and racial disparity with AND	685
Issues noted	Found Williams but not Brown
Exact string: ((((((((((antepartum[Title/Abstract] AND (english[Filter])) OR (ante-partum[Title/Abstract] AND (english[Filter]))) OR ("ante partum"[Title/Abstract] AND (english[Filter]))) OR (intrapartum[Title/Abstract] AND (english[Filter]))) OR (intra-partum[Title/Abstract] AND (english[Filter]))) OR ("intra partum"[Title/Abstract] AND (english[Filter]))) OR (fetal[Title/Abstract] AND (english[Filter]))) OR (foetal[Title/Abstract] AND (english[Filter]))) OR (perinatal[Title/Abstract] AND (english[Filter])) AND (english[Filter])) AND ((((((death*[Title/Abstract] AND (english[Filter])) OR (dead[Title/Abstract] AND (english[Filter]))) OR (mortal*[Title/Abstract] AND (english[Filter]))) OR (wast*[Title/Abstract] AND (english[Filter]))) OR (loss*[Title/Abstract] AND (english[Filter]))) OR (demise[Title/Abstract] AND (english[Filter])) AND (english[Filter])) AND (english[Filter])) OR ((((((((((((stillbirth[MeSH Terms] AND (english[Filter])) OR (fetal death[MeSH Terms] AND (english[Filter]))) OR ("perinatal death"[MeSH Terms] AND (english[Filter]))) OR (perinatal mortality[MeSH Terms] AND (english[Filter]))) OR (pregnancy outcome[MeSH Terms] AND (english[Filter]))) OR (stillb*[Title/Abstract] AND (english[Filter]))) OR (still-b*[Title/Abstract] AND (english[Filter]))) OR ("still born"[Title/Abstract] AND (english[Filter]))) OR ("still borns"[Title/Abstract] AND (english[Filter]))) OR ("still birth"[Title/Abstract] AND (english[Filter]))) OR ("still births"[Title/Abstract] AND (english[Filter]))) OR (deadborn[Title/Abstract] AND (english[Filter]))) OR ("spontaneous termination"[Title/Abstract] AND (english[Filter]))) OR ("spontaneous terminations"[Title/Abstract] AND (english[Filter])) AND (english[Filter])) AND (english[Filter])) AND (((((disparit*[Title/Abstract] AND (english[Filter])) OR (inequit*[Title/Abstract] AND (english[Filter]))) OR (equity[Title/Abstract] AND (english[Filter])) AND (english[Filter])) AND (((((((minority groups[MeSH Terms] AND (english[Filter])) OR ("ethnic groups"[MeSH Terms] AND (english[Filter]))) OR ("population groups"[MeSH Terms] AND (english[Filter]))) OR (race[Title/Abstract] AND (english[Filter]))) OR (racial[Title/Abstract] AND (english[Filter]))) OR (ethnic*[Title/Abstract] AND (english[Filter]))) OR (minorit*[Title/Abstract] AND (english[Filter])) AND (english[Filter])) AND (english[Filter])) OR ((health status disparities[MeSH Terms] AND (english[Filter])) OR ("race factors"[MeSH Terms] AND (english[Filter])) AND (english[Filter])) AND (english[Filter]))	

Table A5: Search results: Scopus

Limits	Hits on 2-20-2021
• LANGUAGE(english) • TITLE-ABS-KEY, which includes keywords also	Will have to apply English limit at the end—can't see how to do it otherwise.
Synonyms for RACE (free text only)	
race	291,954
racial	124,949
ethnic*	371,790
minorit*	184,884
Combine race terms with OR	750,099
Synonyms for DISPARITY (free text only)	
disparit*	156,802
inequit*	23,612
equity	95,959
Combine disparity terms with OR	260,909
Combine race and disparity terms with AND	47,772
Synonyms for STILLBIRTH (free text only)	
stillb*	25,146
still-b*	Does not work, interpreted to allow e.g., "still be … " but also hyphens are ignored in Scopus so the remaining terms in this group will work fine
still born	365
still borns	23
still birth	1,247
still births	1,247
deadborn	5
spontaneous termination	270
spontaneous terminations	270
Combine stillbirth terms with OR	26,448
Synonyms for DEATH (free text only)	
death*	1,347,741
dead	165,193
mortal*	1,490,608
wast*	886,270
loss*	2,537,458
demise	18,402
Combine death terms with OR	5,852,538
Synonyms for FETAL (free text only)	
antepartum	7,843
ante-partum	Not used
ante partum	691
intrapartum	11,470
intra-partum	Not used
intra partum	564
fetal	418,130
foetal	418,130
perinatal	128,651
Combine fetal terms with OR	520,569
Combine fetal and death terms with AND	116,255
Combine fetal/death and stillbirth terms with OR	131,836
Combine fetal death/stillbirth and racial disparity terms with AND	380
Above, with English limit	378
Issues noted	Excellent, got both Williams and Brown
Exact string: ((((TITLE-ABS-KEY (antepartum)) OR (TITLE-ABS-KEY ("ante partum")) OR (TITLE-ABS-KEY (intrapartum)) OR (TITLE-ABS-KEY ("intra partum")) OR (TITLE-ABS-KEY (fetal)) OR (TITLE-ABS-KEY (foetal)) OR (TITLE-ABS-KEY (perinatal))) AND ((TITLE-ABS-KEY (death*)) OR (TITLE-ABS-KEY (dead)) OR (TITLE-ABS-KEY (mortal*)) OR (TITLE-ABS-KEY (wast*)) OR (TITLE-ABS-KEY (loss*)) OR (TITLE-ABS-KEY (demise)))) OR	

Limits	Hits on 2-20-2021
((TITLE-ABS-KEY (stillb*)) OR (TITLE-ABS-KEY ("still born")) OR (TITLE-ABS-KEY ("still borns")) OR (TITLE-ABS-KEY ("still birth")) OR (TITLE-ABS-KEY ("still births")) OR (TITLE-ABS-KEY (deadborn)) OR (TITLE-ABS-KEY ("spontaneous termination")) OR (TITLE-ABS-KEY ("spontaneous terminations")))) AND (((TITLE-ABS-KEY (disparit*)) OR (TITLE-ABS-KEY (inequit*)) OR (TITLE-ABS-KEY (equity))) AND ((TITLE-ABS-KEY (race)) OR (TITLE-ABS-KEY (racial)) OR (TITLE-ABS-KEY (ethnic*)) OR (TITLE-ABS-KEY (minorit*)))) AND (LIMIT-TO (LANGUAGE,"English"))	

Table A6: Search results: Cinahl

Limits	Hits on 2-21-2021
• Do NOT need to include the 'narrower' terms (but ok to) • Do NOT select 'major concepts' • For free text, the Cinahl default is title/abstract/subject so DO NOT NEED TO SPECIFY	English language for all
Synonyms for RACIAL DISPARITY (thesaurus only)	Explode (if possible)
"Health Status Disparities"	8,104
"Race Factors"	25,458
Combine racial disparity terms with OR	32,832
Synonyms for RACE (thesaurus and free text)	
Thesaurus terms	Explode (if possible)
"Minority Groups"	12,253
"Ethnic Groups"	80,413
Free text terms	
race	63,847
racial	22,835
ethnic*	76,720
minorit*	38,556
Combine race terms with OR	187,685
Synonyms for DISPARITY (free text only)	
disparit*	45,891
inequit*	6,562
equity	9,745
Combine disparity terms with OR	56,971
Combine race and disparity terms with AND	20,278
Combine race/disparity and racial disparity terms with OR	46,216
Synonyms for STILLBIRTH (thesaurus and free text)	
Thesaurus terms	Explode (if possible)
"stillbirth"	Not a thesaurus term!
"perinatal death"	8,108
"Pregnancy outcome"	24,363
Free text terms	
stillb*	4,890
still-b*	Doesn't work; hyphenated and spaces are searched simultaneously so the below 4 rows also cover these terms hyphenated
"still born"	20
"still borns"	0
"still birth"	90
"still births"	50
deadborn	0
"spontaneous termination"	34
"spontaneous terminations"	6
Combine stillbirth terms with OR	32,652
Synonyms for DEATH (free text only)	
death*	213,431
dead	7,521
mortal*	304,001
wast*	14,644
loss*	177,931
demise	1,738
Combine death terms with OR	618,861
Synonyms for FETAL (free text only)	
antepartum	1,986
ante-partum	Not needed, hyphen and space are same
"ante partum"	31
intrapartum	5,147

Limits	Hits on 2-21-2021
intra-partum	Not needed, hyphen and space are same
“intra partum”	79
fetal	62,192
foetal	62,192 (seems unneeded)
perinatal	33,090
Combine fetal terms with OR	90,744
Combine fetal and death terms with AND	21,531
Combine fetal/death and stillbirth terms with OR	43,016
Combine fetal death/stillbirth and racial disparity terms with AND	798
Issues noted	Got Williams, not Brown
Exact string: Contact author	

Table A7: Search results: PsycINFO

Limits	Hits on 2-21-2021
• English language • AB OR TI for abstract and title. Keyword is the default if no field is specified • Explode manually • Default "apply equivalent subjects" is fine	English language for all For free text, could not see how to get Ab, ti, and keyword all at once, so every free text term is an OR combination of no field (since default is keyword), Abstract, and Title.
Synonyms for RACIAL DISPARITY (thesaurus only)	Explode if possible
"health disparities"	8,470
"racial disparities"	1,179
"racial and ethnic differences"	33,577 (did NOT explode as this adds "OR race (anthropological)")
Combine racial disparity terms with OR	41,116
Synonyms for RACE (thesaurus and free text)	
Thesaurus terms	Explode if possible
"Race (anthropological)"	5,661
"minority groups"	18,544
"racial and ethnic groups"	108,523
Free text terms	
race	75,957
racial	82,221
ethnic*	136,973
minorit*	62,278
Combine race terms with OR	240,297
Synonyms for DISPARITY (Thesaurus and free text)	
Thesaurus terms	Explode if possible
"equity"	9,904
Free text terms	
disparit*	37,270
inequit*	7,174
equity	18,076
Combine disparity terms with OR	57,934
Combine race and disparity terms with AND	19,501
Combine race/disparity and racial disparity terms with OR	52,484
Synonyms for STILLBIRTH (free text only)	
stillb*	913
still-b*	Didn't work, same as Cinahl; checked that "still born" and "still-born" get the same hits
"still born"	11
"still borns"	1
"still birth"	27
"still births"	19
deadborn	0
"spontaneous termination"	9
"spontaneous terminations"	1
Combine stillbirth terms with OR	968
Synonyms for DEATH (free text only)	
death*	103,208
dead	5,738
mortal*	43,923
wast*	6,048
loss*	124,670
demise	1,541
Combine death terms with OR	247,673
Synonyms for FETAL (free text only)	
antepartum	513

Limits	Hits on 2-21-2021
ante-partum	Not needed, hyphen and space are same
“ante partum”	11
intrapartum	423
intra-partum	Not needed, hyphen and space are same
“intra partum”	14
fetal	14,404
foetal	14,404 (seems unneeded)
perinatal	13,928
Combine fetal terms with OR	27,258
Combine fetal and death terms with AND	3,728
Combine fetal/death and stillbirth terms with OR	4,319
Combine fetal death/stillbirth and racial disparity terms with AND	90
Issues noted	Found Brown ! and not Williams!
Exact string: Contact author	

Table A8: Details of 95 included studies

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
Non-government reports, stillbirth data restricted to 20+ weeks, by author and year, n=46							
Allen 2005[367]	To examine associations between race and gestational age at fetal death in South Carolina to identify sociodemographic risk factors to help refine care protocols	100,670 singleton live births and fetal deaths to white or Black South Carolina residents reported to the SC DOH during 1999-2000	non-residents, multiples, other races	secondary data analysis of a historical cohort using 1999-2000 South Carolina Vital Records birth file to which fetal death file was appended	fetal death	fetal death at 20+ weeks (implied)	*Racial differences in fetal death rates and gestational age at death were not significant after adjustment*
Ananth 2005[368]	To study age, period, and cohort effects on temporal trends in stillbirth in Black and white women	71,037,685 singleton deliveries in the U.S. resulting in a live birth or fetal death between 1981 and 2000	maternal age <15 or 50+ years; birthweight < 500 g or missing; gestational age <20 weeks	U.S. live birth and fetal death registration files assembled by NCHS, including births in the 50 states and DC	stillbirth	fetal death at 20+ weeks	*Blacks were at a 1.2- to 2.9-fold increased risk for stillbirth relative to Whites. Strong effects of age and period on stillbirth trends did not explain the disparity, with attributable fractions of 16.5% and 24.9% (Black women) and 14.5% and 36.2% (white women) for age and period, respectively*
Andrade 2008[128]	To study factors associated with an adverse pregnancy outcome in women with systemic lupus erythematosus (SLE)	102 pregnancy outcomes in patients meeting American College of Rheumatology criteria for classification of SLE, 16+ years of age, with disease duration at enrollment of five years or less, with all grandparents of the same ethnicity, and pregnancy occurring after SLE diagnosis, 2005	ns	LUMINA (Lupus in Minorities: Nature versus Nurture) cohort database	miscarriage, stillbirth, abortion, PTB	death at ≥20 weeks	no disparity found
August 2011[369]	To examine the association between infant mortality and stillbirth during a subsequent pregnancy, and whether there are any racial disparities	Two consecutive births of 20–44 weeks from each mother, totaling 640,700 births (Missouri, 1989-2005)	first or second pregnancies, multiples, sibling pairs, stillbirths in first pregnancy, fetal death in second pregnancy, implausible interpregnancy interval	Missouri maternally-linked cohort dataset with data on livebirths and fetal deaths for each sibling	stillbirth	in utero fetal death at 20+ weeks	*Women with previous infant death were more likely to experience subsequent stillbirth than women with a surviving infant, with the risk nearly twice as high in white women (HR 1.96, 95% CI 1.13, 3.39) and more than four times higher in Black women (HR 4.28, 95% CI 2.61, 6.99)*
Brisendine 2020[153]	To assess evidence for the weathering hypothesis in stillbirth	21,516,830 singleton livebirth and fetal death deliveries to U.S. resident women, 2007-2014	stillbirths at <20 weeks, deliveries <=500 grams	NCHS fetal death and live birth files for 2007–2014	stillbirth	20+ weeks and >500 grams	*Black women aged 40+ had a 3.5 times higher risk of stillbirth than women under 20 (OR 3.47, 95% CI 3.24, 3.70), while for white women, the risk was more than 2.5 times higher (OR 2.68, 95% CI 2.5, 2.82). The disparity in risks peaked at ages 30–34 and then declined*
Brown 2012[81]	To assess associations between residential segregation and stillbirth in	1,419,767 births in Georgia, 1994-2006	ns	GA Office of Health Indicators for Planning of the Department of Community Health, Division of Public Health; U.S. Census;	stillbirth	fetal death >20 weeks	*Increased county segregation was associated with decreased stillbirth risk in white mothers (highest vs. lowest quintile of*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
	Black and white mothers in Georgia			Population Studies Center of the University of Michigan; area-level data were linked to birth outcomes by county Federal Information Processing Standard codes			*segregation, OR 0.82, 95% CI 0.71, 0.94), and decreased stillbirth risk in Black mothers (OR 1.15, 95% CI 0.99, 1.33). Racial disparity rose from an OR of 1.67 (95% CI 1.52, 1.83) for low-segregation counties to 2.35 (95% CI 2.16, 2.55) for high-segregation counties*
Buck 1995[370]	To review spontaneous fetal deaths among white, Black, and American Indian women and assess evidence of variation by cause of death, gestational age at death, or maternal age	973,891 fetal deaths and live births in upstate NY, 1980-1986	missing race, fetal deaths <21 weeks	New York State fetal death registry	stillbirth	fetal deaths at >20 weeks	*Fetal deaths to white and Black mothers were most often at 24-32 weeks, and American Indian fetal deaths at more than 33 weeks. Black teenage mothers experienced the largest proportion of losses (23 percent) compared with white (10 percent) and American Indian (11 percent) teenage mothers*
Cai Hoff and Archer 2007[151]	To carry out a Perinatal Periods of Risk analysis for Jackson County, Missouri, and examine racial differences in fetal-infant mortality	50,975 fetal and infant deaths and live births to residents of Jackson County, Missouri, delivered 2000-2004	terminations	linked birth and death cohorts and selected fetal death records from the Kansas City Health Department which receives them from the Missouri Department of Health and Senior Services	fetal and infant mortality	≥24 weeks' gestation and ≥500 g birthweight	racial disparity in stillbirth not mentioned
Carmichael 2015[371]	To assess evidence for variation of associations between maternal obesity and stillbirth by gestational age, maternal race/ethnicity, and parity	1,125,246 mothers in California, 2007-2010	multiples; <20 or >41 weeks or unknown gestation; congenital or chromosomal abnormalities; missing height or weight; outlier height or weight; race/ethnicity other than white, black or Hispanic; women with pre-gestational diabetes and chronic or gestational hypertension or preeclampsia/ eclampsia	fetal death and live birth certificates and maternal and infant hospital discharge records, linked by the California Office of Statewide Health and Planning	stillbirth	in utero death at 20+ weeks	*The relative risk for stillbirth with a 20-unit change in BMI was significant at 20-23 weeks for NHW, NHB, and Hispanic nulliparous and multiparous mothers; at 24–27 weeks, for multiparous NHW; at 28–31 weeks, for multiparous NHW and nulliparous NHW and NHB; at 32–36 weeks, for multiparous NHW and nulliparous NHB; and at 37–41 weeks, for all except nulliparous NHB*
Carmichael 2019[372]	To compare prevalence of and risk factors for stillbirth and livebirth at peri-viable gestational ages in California, and evidence for variation by race/ethnicity	2,487,468 deliveries at 310 California hospitals, 2007-2011	other or missing race/ethnicity, multiples, gestational age <20 or >41 weeks' gestation, implausible birthweight for gestational age	derived from vital records using files prepared by the California Office of Statewide Hospital Planning and Development including data from fetal death certificates and linked data from live birth and infant death certificates	stillbirth, NND <24 hours after delivery, NND 24 hours-1 year after delivery, livebirths who survived first year	fetal death at 20+ weeks	*Non-white race was associated with increased risk of stillbirth at 20-25 weeks, compared with livebirth at 37-41 weeks*
Copper 1994[132]	To assess associations between demographic, medical, and obstetric risk factors, GA at delivery, and fetal death, in order to	all 34,350 births occurring in 5 perinatal centers in the U.S., 1982-1986	ns	March of Dimes Multicenter preterm birth prevention project database which includes demographic, medical and obstetric data from screening, plus	stillbirth	any birth at 20+ weeks with Apgar of 0 at 1 and 5 mins	*Blacks had greater risk of stillbirth when compared to other women*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
	understand reasons for the slow decline in fetal death rates			medical and obstetric conditions from medical charts			
Demissie 2001[373]	To understand Black-white disparity in preterm birth in relation to neonatal and infant mortality	U.S. births, 1989-1997	ns	NCHS fetal death and linked livebirth and infant death databases	preterm birth, neonatal and infant mortality, fetal death	in utero death at 28+ weeks	stillbirth not mentioned
Dryfhout 2010[143]	To explain how race is related to stillbirth and test a model of social antecedents of behavioral and medical risk factors	stratified systematic random sample of 15,975 live births, late fetal deaths, and infant death vital records from 48 states, DC and NYC, 1988	Hispanic, missing parity or gestational age, preterm livebirths	National Maternal and Infant Health Survey 1988 sponsored by U.S. Department of Health and Human Services, NCHS, which is a nationally representative sample of live births, fetal deaths, and infant deaths including a questionnaire and vital records	stillbirth	fetal loss at 20+ weeks	*Medical and social epidemiological explanations did not reduce racial disparity in stillbirth in this study*
Faiz 2012[374]	To examine stillbirth trends and risk factors by race/ethnicity and nativity in New Jersey	all 937,283 singleton births in New Jersey between 20 and 42 weeks with birthweight ≥500 g, 1997-2005	ns	electronic birth certificate (EBC) records for live births and fetal death certificates linked to hospital discharge records	stillbirth	death of fetus prior to complete expulsion or extraction of a product of conception, where the fetus showed no signs of life such as breathing or beating of the heart, pulsation of umbilical cord, or definite movement of voluntary muscle; all stillbirths at 20+ weeks are reported	*Rates of stillbirth decreased from 3.8 in 1997 to 2.7/1000 total births in 2005 for white NHs but were unchanged for NHB, Hispanic, and other NHs; the risk of stillbirth for black as compared to white NHs was 1.9 (95% CI 1.7, 2.1)*
Getahun 2005[375]	To examine contribution of parental race to adverse perinatal and infant outcomes	all 21,005,786 singleton live births and stillbirths in the U.S., 1995-2001	births <20 weeks and <500 g birthweight, women aged <15 years, missing or "other" maternal or paternal race, implausible birthweight and gestational age	NCHS linked birth/infant death files	SB, PTB, SGA, LGA, infant death	fetal death of 20+ weeks and 500+ g	*Interracial couples had a higher risk of stillbirth than white couples: mother white–father black couples' risk ratio was 1.17 (95% CI 1.10, 1.26) and mother black–father white was 1.37 (95% CI 1.21, 1.54). The relative risk for stillbirth for Black couples was 1.67 (95% CI 1.62, 1.72)*
Getahun 2007[149]	To examine race-specific stillbirth risks by timing (antepartum versus intrapartum)	626,883 singleton livebirths or stillbirths in Missouri, 1989-1997	multiples, <20 or 43+ weeks, races other than white or African American, missing data on stillbirth timing	Missouri live birth and fetal death files assembled by the Missouri Department of Health and Senior Services	AP and IP stillbirth	20-43 weeks	*There was racial variation in risk factors, with increased risk of AP stillbirth with maternal age 35+, lack of prenatal care, pre pregnancy BMI of 30+, and prior preterm or small-for-gestational*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
							age birth in white but not African-American mothers, and increased risk of both AP and IP stillbirth with BMI <18.5 in African-American but not white mothers
Gold 2010[144]	To evaluate risk of fetal death for mixed and same race couples and examine prematurity and low birthweight as possible mediators	1,600,000 singleton pregnancies in California with birthweight >500 g and gestational age >20 weeks, 1998-2002	race missing or reported as multiple race or race other than Black or white, births 46+ weeks, birthweights >14 pounds; women >50 years and men >70 years	California Birth Cohort, which provides birth and death certificate information for all births, fetal deaths, and infant deaths in the state	stillbirth, prematurity, LBW	fetal deaths of 20+ weeks and 500+ g	*Black couples had a higher risk of stillbirth than white couples (OR 2.11, 95% CI 1.77, 2.51), as did black mother-white father couples (OR 2.01, 95% CI 1.16, 3.48) and white mother-black father couples (OR 1.84, 95% CI 1.33, 2.54). Associations were no longer significant when birthweight and gestational age were added to regression models*
Guendelman 1994[175]	To assess racial/ethnic differences in fetal mortality and social and behavioral predictors of fetal death (including Hispanic acculturation) in mothers in California who sought public assistance for prenatal care	80,431 livebirths and stillbirths of California mothers who were recipients of prenatal care, at or below 200% of the federal poverty level, and who lacked public or private insurance for prenatal care, 1984-1989	race other than white or Black; primary language spoken at home other than English or Spanish	California perinatal reporting system, a statewide database with data on all prenatal care recipients at the 97 clinics funded by the CA Dept of Health Services	fetal death	fetal death of 20+ weeks	*Hispanic women had a significantly lower risk of short-gestational stillbirth than NHs, but a higher proportion of Hispanic stillbirths were full-term than was the case in NHs*
Healy 2006[184]	To assess whether early access to prenatal care minimizes racial disparity in perinatal mortality	35,529 pregnant women in 9 states enrolled at 10-13 weeks' gestation, 1999-2002	elective terminations; incomplete demographic data; major structural anomalies or aneuploidy	prospectively collected data from large, multicenter investigation of singleton pregnancies, the FASTER (First- and Second-Trimester Evaluation of Risk) trial	fetal demise at less than 24 weeks, fetal demise at 24 or more weeks of gestation, neonatal demise	fetal demise at 24+ weeks	*The odds of perinatal mortality for Black, Hispanic, and other racial/ethnic groups as compared to whites were 3.5 (95% CI 2.5, 4.9), 1.5 (95% CI 1.2, 2.1), and 1.9 (95% CI 1.3, 2.8), respectively*
Hsieh 1997[376]	To assess the impact of changes in birthweight distribution and birthweight-specific fetal death rates on declines in the crude fetal death rate in the U.S., and to examine racial disparity in the fetal death rate	U.S. live births and fetal deaths, 1979-1990	ns	annual volumes of U.S. vital statistics published by NCHS, including live birth and fetal death files	fetal death	presumed gestation of 20+ weeks	*In 1979-1990, the crude fetal death rate decreased for all racial groups, more so in whites and others (22%) than blacks (10%). In whites, 73.4% of the reduction was attributable to improvement in birthweight-specific fetal death rates, and the remainder to improvement in birthweight distribution. In the black population, the reduction was entirely attributable to improvement in birthweight-specific fetal death rates, while in other groups, improvement in birthweight distribution was the major determinant. Although black births represented 16.5% of all U.S. births, they accounted for 26-29% of the crude fetal death rate*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
Kallan 2001[377]	To examine fetal death rates by nativity and race/ethnicity in New Jersey	796,080 singleton pregnancies with a gestational age of 20 weeks or more in New Jersey, 1991-1998	ns	NJ reports of fetal deaths	fetal death (stillbirth)	fetal death at 20+ weeks	no abstract
Larkin 2018[378]	To determine the effect of sex- and race/ethnicity-specific fetal growth curves on perinatal death rates associated with SGA	all 20,095,735 liveborn and stillborn deliveries registered in the continental U.S., 2005-2009	major congenital anomalies or aneuploidy, multiples, <24 and 42+ weeks, unknown Hispanic origin	NCHS	perinatal mortality	if fetal death certificate was completed at the time of delivery; 24+ weeks	*Using a non-specific birthweight curve, perinatal death rates were higher for NH blacks (20.4/1,000, 95% CI 20.0, 20.8) than non-Blacks (15.9/1,000, 95% CI 15.7, 16.1). This difference increased with use of a race-specific birthweight curve: 29.7/1,000 (95% CI 29.0, 30.3) for SGA blacks and 14.7/1,000 (95% CI 14.6, 14.9) for SGA non-Blacks, respectively*
Lemon 2016[145]	To assess the extent to which obesity may explain Black-White disparity in infant mortality and stillbirth in Pennsylvania	1,058,461 singleton stillbirths and livebirths in Pennsylvania, 2003-2011	missing birthweight, gestational age, sex, or birth facility; gestational age <20 or >42 weeks; self-reported race/ethnicity other than NH Black or NH white; congenital anomalies	Penn MOMS, a population-based study of linked birth-infant death certificates and fetal death certificates in Pennsylvania	stillbirth, IM	20+ weeks gestation	*Compared with NH White women, NH Black women were more likely to have obesity (30 kg/m^2) and experienced a higher rate of stillbirth (8.3 vs. 3.6 stillbirths per 1,000 live-born and stillborn infants) and infant death (8.5 vs. 3.0 infant deaths per 1,000 live births). When the contribution of pre pregnancy obesity was removed, the difference in risk between NH Blacks and NH Whites decreased from 6.2 (95% CI: 5.6-6.7) to 5.5 (95% CI: 4.9-6.2) excess stillbirths per 1,000 and 5.8 (95% CI: 5.3-6.3) to 5.2 (95% CI: 4.7-5.7) excess infant deaths per 1,000. Conclusions: For every 10,000 live births in Pennsylvania (2003-2011), 6 of the 61 excess infant deaths in NH Black women and 5 of the 44 excess stillbirths (2006-2011) were attributable to pre pregnancy obesity*
Lorch 2012[352]	To examine whether higher fetal death rates in minority racial/ethnic groups are mediated by factors that occur later in pregnancy	all 7,104,674 hospital deliveries in California, Missouri, and Pennsylvania at 23-44 weeks between January 1, 1995, and June 30, 2005, including fetal deaths and live births	unmatched records; birthweight <400 g or >8000 g or if birthweight > 5 SD from mean birthweight for gestational age; "other" racial group	fetal death, live birth, maternal hospital discharge and newborn hospital discharge records	fetal death	fetus with gestational age of 23-44 weeks and birthweight >400 g	*For Black women, fetal factors mediated the largest percentage (49.6%; 95% CI 42.7, 54.7) of fetal death disparity; antepartum and intrapartum factors mediated some of the difference in fetal deaths for both Black and Asian women; and socioeconomic factors mediated 35.8% of the disparity (95% CI 25.8%, 46.2%) for Hispanic women*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
Meyer 1999[379]	To examine statewide trends in multiple deliveries and associations with maternal age, birthweight distribution, the low birthweight rate, and fetal and infant mortality rates	Births to residents of North Carolina, 1980-1997	race other than white or Black, therapeutic abortion	North Carolina linked live birth/infant death files and fetal death files	LBW, fetal and infant mortality, multiples	fetal deaths of 20+ weeks	racial disparity in stillbirth not mentioned
Rosenstein 2014[137]	To compare mortality risk of expectant management with risk of infant death at term across race/ethnicity	3,759,300 births in California, 1997-2006	mother/infant pairs with LMP missing or nonsensical; multiples, complications such as diabetes mellitus (preexisting or gestational), chronic hypertension, and congenital anomalies or genetic causes of death; deliveries <37 or >42 weeks; race/ethnicity other or missing	California Vital Statistics Birth Certificate Data, Patient Discharge Data, Vital Statistics Death Certificate Data, and Vital Statistics Fetal Death File. The California Office of Statewide Health Planning and Development, as part of the California Health and Human Services Agency, maintains linked data sets including maternal antepartum and postpartum hospital records, birth records, and all infant admissions in the first year	stillbirth and infant death	ns	*The risk of stillbirth was highest in Black women (18.0 per 10,000 ongoing pregnancies compared with 9.4 in white women, p < 0.001). The composite risk of expectant management only surpassed the risk of delivery at 39 weeks, when the number needed to deliver to prevent one death ranged from 751 (Black women) to 2587 (Asian women)*
Salihu and Kinniburgh 2004[380]	To investigate racial disparities in stillbirth by plurality	14,756,690 singleton, twin, and triplet gestations in the U.S., 1995-1998	ns	"matched multiple birth file" assembled by NCHS covering the period 1995–1998, including matched and linked data for multiple deliveries in the U.S., including individual records of live births and fetal deaths involving multiple deliveries; and the natality and fetal death data files for 1995–1998 for singletons	stillbirth	intrauterine fetal death at 24+ weeks	*The risk of stillbirth was elevated in black compared with white fetuses among singletons (OR 2.9, 95% CI 2.8, 3.0) and twins (OR 1.3, 95% CI 1.2, 1.4) but comparable among triplets (OR 1.2, 95% CI 0.7, 2.1). This decreasing trend by plurality was significant (p for trend < 0.001)*
Salihu and Williams 2004[381]	To determine the magnitude of black-white disparity in mortality among triplets	15,681 U.S. triplets to Black or white mothers for whom there was complete matching and linkage of records, 1995-1997	ns	matched multiple birth file prepared by NCHS	stillbirth, neonatal, perinatal, post neonatal, and infant mortality	intrauterine fetal death at 20+ weeks	*The stillbirth risk for Black and white triplets was comparable*
Salihu 2005[382]	To assess fetal and infant mortality outcomes by race/ethnicity and plurality	37,489,600 live births and fetal deaths of 20-44 weeks in the U.S., 1995-2000	ns	"matched multiple birth file" assembled by NCHS covering the period 1995–2000, containing matched and linked data for multiple deliveries including individual records of live births and fetal deaths involving multiple deliveries; natality and fetal death data files for 1995–2000 for analyses on stillbirth involving singletons; and linked birth/infant files up to 1999 for infant mortality among singletons	stillbirth and infant mortality	fetal death at 20+ weeks	*Among singletons, stillbirth (OR 0.91, 95% CI 0.90, 0.92) was lower in Hispanics than in whites; among twins, the risk was comparable (OR 1.06, 95% CI 0.98, 1.13); but Hispanic triplets had a 50% higher likelihood of dying in utero than white triplets (OR 1.50, 95% CI 1.06, 2.14)*
Salihu 2006[146]	To assess whether prior cesarean delivery is a risk factor for stillbirth, including any racial variation	396,441 second pregnancies to Missouri women who had 2 sequential singleton pregnancies beyond 20 weeks,	gestational age outside 20-44 weeks, congenital anomalies	Missouri maternally linked cohort data with data on both live birth and fetal death for each sibling	stillbirth	in utero fetal death at 20+ weeks	*Among whites, the stillbirth risk in women with vs without prior cesarean delivery was not significantly different (OR 1.0,*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
		with first pregnancy liveborn, 1978-1997					*95% CI 0.9, 1.2), but it was elevated among Blacks (OR 1.4, 95% CI 1.1, 1.7)*
Salihu 2007[187]	To estimate the risk of stillbirth by obesity subtype and race	1,413,953 singleton pregnancies in Missouri within 20–44 weeks, 1978-1997	multiples; records for which BMI could not be computed; underweight mothers	Missouri maternally linked cohort data files	stillbirth	in utero fetal death at 20+ weeks	*Obese black mothers experienced more stillbirths than their white counterparts (HR 1.9, 95% CI 1.7, 2.1, and HR 1.4, 95% CI 1.3, 1.5, respectively). The black disadvantage in stillbirth widened with increase in BMI, with the greatest difference observed among extremely obese black mothers (HR 2.3, 95% CI 1.8, 2.9)*
Salihu 2009[383]	To identify Black-white differences in risk profiles for early and late stillbirth among women with low BMI	430,130 singleton deliveries in Missouri within 20-44 weeks, 1989-1997	BMI that was missing or implausible; race other than Black or white	Missouri maternally linked cohort data files	stillbirth	in utero fetal death of 20+ weeks	*Underweight black mothers had comparable risks for total (OR 0.9, 95% CI 0.7, 1.2), early (OR 1.1, 95% CI 0.8, 1.5), and late stillbirth (OR 0.8, 95% CI 0.5, 1.2) compared to their normal-weight counterparts; underweight white gravidas had a 30% reduced likelihood of late stillbirth vs normal-weight mothers (OR 0.7, 95% CI 0.6, 0.9), while risks for total and early stillbirth were not significant*
Sharma 2006[384]	To test whether women with prior stillbirth have elevated risk for subsequent stillbirth, and whether this is differential by race	404,180 singleton births of 20–44 weeks in Missouri to mothers who delivered both first and second consecutive singletons, 1978-1997	single pregnancies (no siblings)	Missouri maternally-linked cohort data files	stillbirth	intrauterine fetal death at 20+ weeks	*Whites had lower risk for stillbirth recurrence than African Americans (OR 2.6, 95% CI 1.2, 5.7)*
Singh 2018[138]	To examine induction of labor by race/ethnicity	143,634 singleton pregnancies with vertex presentation delivering at 24+ weeks in women not undergoing pre-labor Cesarean, without placenta previa, and in whom labor onset was known, in 12 clinical centers across nine ACOG districts, 2002-2008	missing race, unknown indication for induction, site with incomplete data, post-term	NICHD-supported Consortium on Safe Labor, a multicenter, retrospective cohort study including labor and delivery data in electronic medical records from 12 clinical centers (with 19 hospitals) across nine ACOG U.S. districts, and surveys on hospital and physician characteristics at each site	induction of labor, indication	ns	*All racial/ethnic groups had lower odds of induction compared with NH white (NHW) women. At term, NHW women had the highest percentage rate (45.4%) of non-medically indicated or induction with no indication ($p < 0.001$). As labor induction may reduce stillbirth, this finding is relevant for the increased risk of stillbirth for NHB women at term*
Timofeev 2014[136]	To determine whether recurrent spontaneous preterm birth differs by race in women receiving 17α-hydroxyprogesterone caproate	7,108 high-risk pregnant women enrolled in a 17α-hydroxyprogesterone caproate home administration program provided by the Women's and Children's Health division of Alere Health, initiating the program at 16.0 to 26.9 weeks, delivering between January 2006 and May 2011, commercially insured or	ns	clinical data collected prospectively from patients and providers	recurrent spontaneous preterm birth <34 weeks, pregnancy loss, C-section, stillbirth, gestational age	ns	stillbirth not mentioned

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
		Medicaid recipients, with singleton gestation, history of prior spontaneous preterm birth, documented pregnancy outcomes, and self-reported African-American or Caucasian race					
Tyler 2012[11]	To determine how fetal death reporting requirements influence variation in early neonatal and fetal mortality rates and racial disparity	all 11,016,103 singleton live births and fetal deaths to NH white and NH black maternal residents of the U.S., 2000-2002	maternal race of Hispanic origin or not listed; births <20 weeks; missing gestational age	birth and linked infant death and fetal death records from the National Center for Health Statistics (NCHS) Division of Vital Statistics	early neonatal mortality rates, fetal mortality rates	20+ weeks	*States with birthweight-alone fetal death thresholds substantially underreported fetal deaths at lower gestations and slightly overreported neonatal deaths at older gestations. This finding was reflected by these states having the highest neonatal mortality rates and racial disparities, but the lowest fetal mortality rates and racial disparities*
Vintzileos 2002[185]	To determine the impact of prenatal care on fetal death and the relation to obstetric and medical high-risk conditions and racial disparity	10,560,077 live births and fetal and infant deaths up to 1 year, registered in all states and DC, at or beyond 24 weeks, 1995-1997	multiples; congenital or chromosomal abnormalities; missing gestational age; birthweight <500 g; missing data on prenatal care	National perinatal mortality datasets assembled by NCHS	fetal death	fetus with no signs of life at birth, at 24+ weeks and 500+ grams	*Fetal death rates were higher for blacks than whites in the presence (4.2 versus 2.4 per 1000) and absence (17.2 versus 2.5 per 1000) of prenatal care. Lack of prenatal care increased the relative risk for fetal death 2.9-fold in blacks and 3.4-fold in whites*
Williams 2018[64]	To examine race-specific associations between segregation and stillbirth	121,754 births to Black or white mothers from 14 hospitals in 12 Hospital Reference Regions, 2002-2008	multiples, missing exposure data, pregnancies from Utah	Consortium on Safe Labor (CSL) is an electronic medical record-based national retrospective cohort study from 2002 to 2008, which included 19 hospitals in 15 Hospital Reference Regions (HRR). Hospitals were selected based on availability of electronic medical records, and because the geographic distribution of the hospitals matched all United States districts of the American College of Obstetricians and Gynecologists	stillbirth	fetal death at 23+ weeks as reported in medical records supplemented with ICD-9 codes	*Low and decreasing levels of segregation were associated with decreased odds of stillbirth, with blacks benefitting more than whites. Decreasing segregation may prevent 900 stillbirths annually among U.S. blacks*
Willinger 2009[4]	To determine the contribution of maternal and fetal characteristics to gestational age and racial differences in stillbirth hazard	5,138,122 singleton gestations delivered at 20–41 weeks in 2001 in 36 states with at least 80% complete reporting for Hispanic origin, method of delivery, and prenatal care history (AL, AZ, AR, CA, CO, CT, DE, ID, IL, IN, IA, KS, KY, LA, MD, MI, MN, MS, MO, MT, NE, NH, NJ, NM, NC, ND, OH, OR, SC, SD, TN, TX, UT, WV, WI, WY)	maternal medical conditions (including anemia; diabetes; cardiac, lung, or renal disease; or chronic hypertension); pregnancy conditions (including incompetent cervix, premature rupture of membranes, uterine bleeding, pregnancy-associated hypertension, or	NCHS Perinatal Mortality Data Files and Birth Cohort Linked Birth/Infant Death Data Sets	stillbirth	fetal death at 20+ weeks	*The black/white disparity in stillbirth hazard at 20–23 weeks was 2.75 (95% CI 2.62–2.88), decreasing to 1.57 (95% CI 1.41–1.75) at 39–40 weeks. Higher education reduced the hazard for whites more than Blacks and Hispanics; medical, pregnancy, and labor complications accounted for 30% of the hazard in Blacks vs 20% in whites and Hispanics; congenital anomalies and SGA contributed more to*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
			eclampsia); labor conditions (including fever, abruption, cord abnormality, placenta previa, or other bleeding); small-for-gestational-age, congenital anomalies				*preterm stillbirth risk among whites than Blacks; and pregnancy and labor conditions contributed more to preterm stillbirth risk among Blacks than whites*
Wingate 2006[177]	To examine the role of fetal death in racial/ethnic variation in perinatal outcomes	17,879,923 single fetal deaths (20+ weeks) to U.S. resident mothers with reported race/ethnicity, 1995-1999	ns	NCHS U.S. Perinatal Mortality files and single live births from Linked Live Birth-Infant Death files	fetal and neonatal death	20+ weeks	*Two-fold disparities between Whites and Blacks persisted for fetal death. Hispanics were less likely than Whites to be reported as a fetal versus hebdomadal (< 7 days) death*
Wingate 2011[385]	To examine changes in gestational-age specific fetal death, first day death, and perinatal death by race/ethnicity	12,921,506 singleton deliveries to NH white, NH black, and Hispanic mothers at 20+ weeks, 1990-1991 and 2001-2002	NM, SD, TN births; implausible or missing values for birthweight or gestational age; birthweight value inconsistent with gestational age	NCHS linked live birth and infant death cohort files and fetal death files	fetal death and first day death	fetal deaths at 20+ weeks	*From 1990 to 2002, the fetal mortality rate among whites and Hispanics declined 4.32% and 12.82%, respectively; for blacks, the rate increased 4.06%, and the black:white fetal mortality rate ratio increased from 2.17 to 2.36. Gestational age-specific black:white combined fetal-first day mortality rate ratios were greater than 1 at later gestational ages (36 weeks on)*
Wingate 2012[186]	To examine how changes in maternal, sociodemographic, and medical risk factors influence changes in fetal, first day, and perinatal mortality, and racial/ethnic variation	11,353,250 live births and fetal deaths to U.S. resident white and Black mothers at 20+ weeks and >500 grams, 1995-1996 and 2001-2002	Hispanic ethnicity	Health Statistics linked live birth and infant death cohort files and fetal death files	first day and fetal mortality	20+ weeks and >500 grams	*Odds ratios for fetal mortality among Blacks (OR 0.97, 95% CI 0.92, 1.02) indicated no change from 1995 to 2002. Among women with modifiable risk factors (smoking, hypertensive disorders, diabetes), the RORs indicated no change in racial disparities over time*
Wingate 2015[386]	To compare fetal and early neonatal outcomes of American Indians/Alaska Natives (AIAN) with non-AIAN groups, including changes in deliveries, maternal characteristics, fetal and early infant death, and cause of death	29,786,071 singleton deliveries to U.S. resident NH American Indian/Alaska Native, NH white, NH black, and Hispanic mothers at 20+ weeks and >500g, 1995-1998 and 2005-2008	missing or unknown Hispanic origin or race, missing data on other covariates	NCHS data from fetal death and live birth–infant death cohort files	fetal mortality, first day mortality, perinatal mortality, cause-specific mortality	fetal death at 20+ weeks and >500 g	*From 1995 to 2008, late fetal death decreased for AIAN (OR 0.83, 95% CI 0.72, 0.97) but increased for Hispanics (OR 1.47, 95% CI 1.40, 1.55). For AIANs compared to whites, increased risk persisted for mortality due to congenital anomalies (ROR 1.28, 95% CI 1.03, 1.60). For blacks compared to AIANs, increased risk of fetal death persisted (2005–2008: OR 0.60, 95% CI 0.53, 0.68), as did lower risk for Hispanics compared to AIANs, although this protective effect declined over time*
Wingate 2017[387]	To examine gestational age-specific fetal mortality with a	all 17,787,576 singleton U.S. livebirths regardless of birthweight or gestational age	multiples, births with out-of-range,	U.S. fetal death and live birth data files maintained by the National Vital Statistics System	fetal death	fetal deaths at 20+ weeks and greater	*There were lower risks of fetal mortality among NHB women (Prevalence Rate Ratio, PRR,*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
	focus on racial/ethnic disparity	and singleton U.S. fetal deaths at 20+ weeks and >500 grams, 2009-2013	inconsistent, or missing gestational age			than 500 grams	*0.76, 95% CI 0.71, 0.81) and Hispanic women (PRR 0.89, 95% CI 0.83, 0.96) compared with NHW at 22-23 weeks. For NHB women, the risk was higher starting at 32-33 weeks (PRR 1.11, 95% CI 1.04, 1.18) and continued to increase with gestational age. Hispanic and AIAN women had lower risks of fetal mortality compared with NHW women until 38-39 weeks.*
Xu 2009[388]	To estimate costs associated with racial disparity in preterm birth and preterm fetal deaths in Michigan	111,264 NH Black and NH White singleton births in Michigan in 2003 with a reported gestational age of 20+ weeks	unknown gestational age	linked hospital discharge and live birth certificate file, infant death records, and fetal death data from Perinatal Mortality Data file issued by NCHS	costs of PTB, fetal death	fetal deaths of 20+ weeks	*1,184 NH Black, singleton preterm births and preterm fetal deaths would have been avoided in 2003 had their preterm birth rate been the same as Michigan NH Whites. Economic costs associated with these excess Black preterm births and preterm fetal deaths amounted to $329 million (range $148-$598 million) across their lifespan above costs of term birth, including costs of initial hospitalization, productivity loss due to death, and major developmental disabilities*
Yuan 2005[389]	To assess changes in gestational age-specific fetal death risk and the extent to which these are due to changes in registration practices and induction of labor	all 1,809,026 singleton pregnancies of 20-43 weeks in 1991 and 1997 in 39 U.S. states and DC	implausible birthweight-GA data, multiples, missing data; states with <80% complete data on maternal medical conditions, lifestyle risk factors, and obstetric procedures; CA, HI, IN, LA, MD, MA, NY, OK, SD (lack of data on smoking); IL (high missingness for induction); and TX (high missingness for smoking); race other than NH white and NH Black	NCHS live birth and fetal death files	gestational age-specific fetal death	fetal deaths 20+ weeks	*The reduced risk of fetal death at 40-43 weeks in 1997 vs 1991 in NH whites (RR 0.79, 95% CI 0.74, 0.84) disappeared after adjusting for induction of labor (risk ratio 0.98, 95% CI 0.82, 1.16). In NH Blacks, this effect of induction of labor was only in high-risk mothers*
Non-government reports, stillbirth data not restricted to 20+ weeks, by author and year, n=17							
Akobirshoev 2019[390]	To assess racial/ethnic disparities in adverse birth outcomes and labor and delivery-related charges among women with IDD	2,110 delivery-related hospitalizations to white, Black or Hispanic women with IDD in a 20% stratified sample of U.S. community hospitals from 37 to 46 states	missing race/ethnicity	Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS), the largest all-payer, publicly-available U.S. inpatient healthcare database, with data on 8 million hospital stays annually from 1000 hospitals	C-section, PTB, stillbirth, SGA, labor- and delivery-related charges	ICD-9 codes 656.4, 656.40, 656.41, 656.43, 768.0, 768.1,	*Significant disparities in stillbirth among NHB and Hispanic women with IDD vs NHW mothers (OR 2.50, 95% CI 1.16, 5.28, $p < 0.01$; OR 2.53, 95% CI 1.08, 5.92, $p < 0.01$, respectively)*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
		(depending on year), 2004-2011				V27.1, V27.3 or V27.4	
Barfield 1996[391]	To examine racial disparities in birth and neonatal outcomes in military personnel in California (a population with minimal financial barriers to healthcare services)	All 2,171,147 fetal deaths and live births in California, 1981-1985	multiples; birthweight < 500 g	Linked birth, fetal, and infant death certificate files from Maternal and Child Health Data Base of the Community and Organization Research Institute, UC-Santa Barbara	fetal and neonatal death, birthweight, prenatal care use	fetal death with birthweight >500g	*Rates of fetal mortality among Black mothers were elevated in both military and civilian groups in comparison with white mothers*
Brown 2007[392]	To assess evidence for the Hispanic paradox in perinatal outcomes	10,755 African American, white, and Hispanic women who used Medicaid for delivery costs and delivered at Duke University Medical Center (DUMC) in Durham, NC, 1994-2004; if >1 birth in the cohort, only the first birth was included	non-Medicaid recipients, non-NC residents, missing medical data, >1 delivery in a calendar year, unknown race/ethnicity, age <11 years	Duke University birth database which has detailed demographic, cost, health service, and outcomes data for all admissions for women who gave birth at DUMC	preeclampsia, gestational diabetes mellitus, placental abruption, preterm birth, SGA, fetal death/stillbirth, maternal death	ICD-9 codes 656.4, 768.0, 768.1, V27.1, V27.3, and V27.4	*African-American women had higher rates of stillbirths than white women*
Cai, Hoff and Okah 2007[393]	To examine evidence for Black-white disparity in fetal deaths late in gestation using gestational age- and weight-specific comparisons	104,449 singleton fetal deaths and livebirths to NH black and NH white mothers in Clay, Jackson and Platte counties in the Kansas City, MO metropolitan area, 1996-2004	other racial/ethnic groups	Kansas City Health Department electronic databases on resident live births and fetal deaths, provided by the Missouri Department of Health and Senior Services	fetal death	involuntary loss in which the fetus showed no evidence of life (i.e., no heartbeat or respiration) on delivery, at 20+ weeks or birthweight 350+ g	*Fetal death rates were higher for NH whites at <28 weeks gestation and at birthweight <1,000 g, and higher for NHB at 32+ weeks and at birthweight 2,500+ g*
Dumas 2020[178]	To examine differences in white and Black teen pregnancy and birth rates in Louisiana Medicaid enrollees	pregnancy outcomes of 1,694 Louisiana women aged 15-17 in 2014 with at least 2 years of Medicaid enrollment	race/ethnicity other than NHB and NHW	Louisiana Medicaid claims	pregnancy outcomes (live vs non live birth)	ICD-9 630-639.9, 656.40-656.43, 768.0, 779.6, V27.1, V27.4-V27.7; ICD-10 O00-O04.89, O08-O08.9, O36.4, P95, Z33.2, Z37.1, Z37.4; CPT 59,812-59,856	no disparity found
Gregory 2003[139]	To evaluate differences between age and race/ethnicity for pregnancy-related complications that affect labor management and obstetric outcomes	443,532 women in labor and at risk for emergency primary Cesarean delivery in California, 1995	previous Cesarean delivery or elective primary Cesarean delivery without labor; uncertain or missing age; delivery in	California Office of Health Planning and Development birth reports	pregnancy-related complications (31 maternal, fetal, and	ns	stillbirth not mentioned

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
			extremely low-volume hospitals		placental ICD codes)		
Kramer 2002[176]	To examine intercountry differences in infant mortality and birthweight distribution, as well as differences in classification of deaths as fetal vs. infant deaths, and under-registration of borderline-viable infants	7,402,554 live births, stillbirths and infant deaths registered in U.S., 1987-1988 (also births in Israel and Norway)	U.S. births that were neither white nor Black	population-based International Collaborative Effort on Perinatal and Infant Mortality country data files based on national-level files of linked birth and infant death certificates	LBW rates, IMR, fetal mortality rates	varied depending on state; for most states, fetal deaths >20 completed weeks; exceptions: Kansas (>350 g), New Mexico and South Dakota (>500 g), and Tennessee (>500 g or, if birthweight unknown, >22 weeks)	*For borderline-viable infants, fetal deaths as a proportion of all perinatal deaths varied between U.S. Blacks (40.3% for births <500g and 37.6% for births 500-749 g) and whites (51.9% and 43.1%, respectively), with larger variation in comparison to Norway and Israel*
MacDorman 2011[394]	To provide an overview of trends in fetal mortality, preterm birth, and infant mortality, including racial/ethnic disparities	all 6,400,000 pregnancies in the U.S., 2005	ns	birth certificates, death certificates, and reports of fetal death filed in state vital statistics offices and transmitted to NCHS	fetal and infant death and PTB	fetal deaths of 20+ weeks	*There are substantial race and ethnic disparities in fetal mortality, with NH black women at greatest risk, followed by American Indian and Puerto Rican women*
Nabukera 2009[395]	To examine racial differences in first and second pregnancy perinatal outcomes and interpregnancy interval (IPI) patterns among women initiating childbearing at ages greater or less than 30	239,930 infants and their mothers aged 20–50 at first pregnancy with two consecutive singleton pregnancies in Missouri during the study period 1978-1997	ns	Maternally-linked live birth/fetal death and infant death files	FD, LBW, and SGA, PTB	death of fetus 20+ weeks or 500+ g	stillbirth not mentioned
Rammah 2019[148]	To examine the risk of stillbirth associated with maternal O3 exposure in Harris County, Texas, and examine differences by race/ethnicity and gestational age	all 358,366 singleton livebirths and stillbirths to mothers residing in Harris County, Texas, 2008-2013	missing gestational age and weight, gestational ages outside 20–44 weeks, births with implausible birth weight–gestational age data and conception dates >20 weeks before study start and < 44 weeks before study end	Texas Department of State Health Services and Texas Commission on Environmental Quality	stillbirth	unintended intrauterine fetal death of 350+ grams or, if weight unknown, of 20+ weeks	*The increased stillbirth risk associated with a 3.6-parts-per-billion increase in O3 exposure was higher for Hispanic (HR 1.14, 95% CI 1.02, 1.27) than for NHB or NHW women*
Reddy 2010[396]	To identify risk factors for antepartum stillbirth and estimate their relative contribution stratified by parity and to determine if these can be used to identify higher risk women	all 174,809 singleton deliveries at 23+ weeks enrolled at 12 clinical centers and 19 hospitals representing nine ACOG districts; only included the first pregnancy enrolled, 2002-2008	births at two institutions with high missingness in medical history data; multiples, stillbirths that were intrapartum or with timing not specified, maternal age missing	Consortium on Safe Labor (CSL), a study conducted by NICHD with electronic medical records from included institutions, such as neonatal intensive care unit data linked to newborn records and maternal and newborn discharge ICD-9 codes	antepartum stillbirth	no signs of life prior to labor with Apgar scores 0/0	*Black race and Hispanic ethnicity were associated with stillbirth. The risk of term stillbirth for women who were white, 25–29 years old, normal weight, multiparous, no chronic hypertension, and no preexisting diabetes was 0.8 per 1,000. Term*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
							stillbirth risk increased with black race (1.8 per 1,000)
Rush 1972[397]	To assess the role of smoking on offspring mortality	3,276 consecutive pregnant patients registered prior to the 21st week of gestation at the Boston City Hospital Prenatal Clinic, 1961-1962	women who did not speak English; missed and incomplete abortions	registration and obstetrical records	birthweight, gestational age, perinatal mortality	fetal death >19 weeks	*Smokers had an excess perinatal loss of 34.4%; excess loss was higher among Black mothers*
Sapra 2017[141]	To evaluate the extent to which selection bias from induced termination affects estimates of racial disparity in preterm delivery	1,593,256 live births, induced and spontaneous terminations of pregnancy in NYC, 2000-2012	race/ethnicity other than NHW or NHB	NYC Bureau of Vital Statistics including live birth data from birth certificate records and data on spontaneous and induced terminations from standardized forms completed by hospital staff	PTB	ns	stillbirth not mentioned
Schummers 2019[398]	To assess risk of adverse birth outcomes by maternal age at first birth and race	all 16,514,849 births to nulliparous women in the U.S., 2004-2013	fetal deaths <20+ weeks or with birthweight <350 g	Birth Cohort-Linked Birth-Infant Death Data Files and Fetal Death Data Files from NCHS	multiple gestation, Caesarean delivery, preterm birth, small for gestational age, stillbirth, neonatal mortality, post neonatal infant mortality	fetal death at ≥20 weeks or birthweight 350+ g	racial disparity in stillbirth not mentioned
Tan 2004[399]	To assess the association between race and fetal and infant death in twins	all 249,221 twins born in the U.S., 1995-1997	race other or unknown; missing death data	matched multiple birth file created by CDC	fetal and infant death	stillbirth 350+ g, or if weight was unknown, 20+ weeks	*Combined fetal and infant mortality in twins was highest for black vs white parents (relative risk, RR, 1.66, 95% C1 1.58, 1.75), and intermediate for white fathers and Black mothers (RR 1.18, 95% Cl 0.92, 1.51) and Black fathers and white mothers (RR 1.37, 95% Cl 1.19, 1.58)*
Witt 2012[140]	To determine whether and how preconception mental health affects adverse maternal and pregnancy outcomes	2,671 women with singleton pregnancies included in the eleven panels of the Pregnancy Detail Files of the Medical Expenditure Panel Survey (MEPS) with nonzero weight and complete covariate data who delivered in 1996-2006; if >1 pregnancy was eligible, a random number generator was used to randomly select a single pregnancy for inclusion	abortions	household component of the 1996–2006 MEPS, a nationally representative sample of the civilian, non-institutionalized population of the U.S.	non-live birth, pregnancy complications, LBW	ns	*Significant racial and ethnic disparities existed for non-live births*
Zhang 2013[400]	To estimate excess adverse pregnancy outcomes by race/ethnicity, and the potential savings for Medicaid paid claims for costs of disparities in these outcomes	1,472,912 women with singleton deliveries in 2006-2007 in 14 southern states (AL, AR, FL, GA, KY, LA, MD, MO, MS, NC, SC, TN, TX, VA) whose Medicaid inpatient claims had a maternal delivery code	American Indian, Asian, and Pacific Islander mothers	Medicaid Analytic eXtract files on inpatient hospital data, which combine Medicaid data from each state, including inpatient, outpatient (and other services), and prescription claims files linked to the personal summary file for each enrollee	adverse pregnancy outcomes: preeclampsia, GDM, abruption, preterm birth, SGA, fetal	fetal death/ stillbirth ICD-9 codes: 656.4, 768.0, 768.1, V27.1, V27.3, V27.4	*African-American women were more likely to experience fetal death/stillbirth than other racial/ethnic groups. Eliminating racial disparities in adverse pregnancy outcomes (not counting infant costs) could generate Medicaid cost savings of*

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					death/stillbirth, maternal death		*$114-$214 million per year in 14 states*
Non-government reports, unknown whether stillbirth data was restricted to 20+ weeks, by author and year, n=16							
Clowse 2016[401]	To identify racial and ethnic disparities in underlying maternal disease, maternal illness and treatment at delivery, and obstetric complications for women with lupus in the U.S.	all 12,524,118 delivery-related hospital discharge records from the Nationwide Inpatient Sample (NIS) in 2008-2010	ns	NIS from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality, which samples 20% of discharges from >1,000 U.S. hospitals	baseline medical disease, medical illness at delivery, and obstetric complications	ns	stillbirth not mentioned
Creanga 2017[402]	To update national pregnancy-related mortality estimates and examine characteristics and causes of pregnancy-related deaths	2,009 pregnancy-related maternal deaths in the U.S. of women 12–55 years who died during or within 1 year of pregnancy, 2011-2013	ns	data from the CDC's Pregnancy Mortality Surveillance System, including death certificates for pregnancy-related deaths and linked birth or fetal death certificates submitted to the CDC's Division of Reproductive Health by the states, NYC and DC; computerized searches of Lexis Nexis; reports by public health agencies, including state-based maternal mortality review committees; professional organizations; and individual healthcare providers	causes of pregnancy-related deaths	ns	stillbirth not mentioned
Emeruwa 2020[131]	To evaluate infection rates and perinatal outcomes among pregnant women with Covid by race/ethnicity	673 women delivering at two New York-Presbyterian–affiliated hospitals in Manhattan, 2020	ns	NY Presbyterian electronic medical records	perinatal outcomes	ns	no abstract
Gould 2003[403]	To compare demographic and socioeconomic risk factors and perinatal outcomes of foreign-born Asian Indian and Mexican mothers to U.S.-born white NH and Black women in California	1,057,976 mothers in California, 1995-1997	U.S.-born women other than Black or white	California linked infant birth/death certificate files	low birthweight, intrauterine growth retardation, preterm birth, fetal death, neonatal death, post neonatal death	ns	*Infants of U.S.-born Black women had the highest rates of fetal mortality in comparison to foreign-born Asian Indian and Mexican and U.S.-born white mothers. Foreign-born Asian Indian women also had a higher incidence of fetal death than U.S.-born whites*
Grant 2017[404]	To assess associations between Black race and gestational age at delivery in twins, and racial variation in adverse pregnancy and neonatal outcomes	535 women with uncomplicated twin gestations who self-identified as NH black or NH white, in 14 clinical sites, 2004-2006	major congenital anomalies, spontaneous fetal death after 12 weeks, monoamniotic twins, suspected twin–twin transfusion syndrome, marked growth discordance, major uterine anomalies, cerclage or planned cerclage, major chronic medical diseases, and twins resulting from	secondary analysis of data from multicenter, prospective double-blind randomized controlled trial of 17-α hydroxyprogesterone caproate versus placebo for the prevention of PTB conducted by the NICHD Maternal-Fetal Medicine Units Network	gestational age at delivery and other pregnancy and neonatal outcomes, including a composite of major neonatal morbidity (diagnosis of at least one of the following complications before initial hospital discharge: fetal	ns	stillbirth not mentioned

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
			intentional fetal reduction		or neonatal death, grade III or IV intraventricular hemorrhage, periventricular leukomalacia, bronchopulmonary dysplasia, or necrotizing enterocolitis stage II or III)		
Izmirly 2011[134]	To determine the mortality and morbidity of cardiac neonatal lupus, NL, and associated risk factors	325 cardiac neonatal lupus cases identified by the Research Registry for Neonatal Lupus and enrolled by September 30, 2010, entailing documentation of maternal antibodies reactive with SSA/Ro and/or SSB/La, confirmation of cardiac NL, and/or presence of cardiac injury or cardiomyopathy (data from 1963-2010)	born with isolated first-degree heart block or isolated sinus bradycardia; unknown gestational age at birth	Research Registry for Neonatal Lupus	morbidity and mortality in cardiac neonatal lupus	ns	*There was a significantly higher case fatality rate in minorities compared with whites*
Parikh 2014[133]	To compare maternal and neonatal outcomes between HIV+ and HIV- mothers and assess racial disparities in pregnancy outcomes in HIV+ women	all 178,972 singleton pregnancies in the U.S. with documented maternal HIV status, race, and antepartum admission; only first documented pregnancy if >1, 2002-2008	chronic medical conditions (e.g., pre-existing diabetes, chronic hypertension, cardiac disease, asthma, renal disease)	Consortium of Safe Labor which includes obstetric and neonatal data from electronic medical records of 19 hospitals at 12 institutions, representing university- and community-based practices across the U.S.	labor and delivery and neonatal outcomes: gestational age, gestational diabetes, hypertensive disease of pregnancy, type of onset of labor, premature rupture of membranes, epidural and oxytocin use, mode of delivery, rates of malpresentation, presence of another sexually transmitted infection (STI), placenta previa, placental abruption, severe maternal perineal lacerations, postpartum	ns	stillbirth not mentioned

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
					hemorrhage, need for blood transfusion, intensive care unit (ICU) admission, endometritis, wound separation or infection, birthweight, Apgar score, neonatal ICU (NICU) admission, length of NICU stay, neonatal fever, stillbirth, perinatal mortality		
Scott 1997[405]	To identify trends in severe complications of pregnancy and their fiscal impact in California	all 4,129,234 delivery and non-delivery hospitalizations for pregnancy complications in California, 1978-1992	ns	California Pregnancy Complication Surveillance System, which uses hospital discharge data provided by the California Office of Statewide Health Planning and Development and includes information on all acute-care civilian hospital admissions and discharges in California	severe complications of pregnancy	ns	stillbirth not mentioned
Shahul 2015[406]	To ascertain racial/ethnic differences in incidence of preeclampsia/ eclampsia, and in maternal comorbidities and complications of pregnancy and delivery, and maternal and fetal mortality, in women with preeclampsia and eclampsia	all 1,175,046 weighted patient discharges from the Nationwide Inpatient Sample (NIS) with a diagnosis of preeclampsia/eclampsia, 2004-2012	ns	NIS which randomly samples 20% of all discharges from all hospitals in the Healthcare Utilization Project (HCUP) of the Agency for Healthcare Quality and Research, including data on 8 million hospital stays annually; national estimates obtained by weighting NIS data to provide estimates for 95% of all U.S. inpatient hospitalizations	inpatient mortality during hospitalization, IUFD	fetal demise during hospitalization	*When compared to white women with preeclampsia, AA women had an increased odds of IUFD (OR 2.45, 95% CI 2.14, 2.82), while the odds of IUFD among Hispanic women did not differ from that for white women*
Silva 2006[129]	To examine ethnic differences in perinatal outcome of gestational diabetes mellitus and identify maternal and fetal factors associated with fetal macrosomia, including ethnicity	2,155 patients with GDM treated in the Sweeter Choice outpatient diabetes program at Kapi‘olani Medical Center, Hawai'i and delivering at term (1995 and 2005)	pregestational diabetes, multiples, coexisting medical conditions such as hypertension, lupus, thyroid disease, and asthma; incomplete information for neonatal weight and neonatal hypoglycemia; ethnic classifications other than Native	Medical records from Kapi‘olani Medical Center	neonatal weight, neonatal hypoglycemia, fetal demise, fetal anomalies, shoulder dystocia, fetal distress, birth asphyxia, polycythemia, hyperbilirubinemia, respiratory distress	ns	stillbirth not mentioned

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
			Hawaiian/Pacific Islander, Japanese, Chinese, Filipino, and Caucasian		syndrome, sepsis, fetal macrosomia		
Soffer 2018[407]	To examine twin pregnancies of mothers with similar access to health care to determine whether race remains a risk factor for adverse pregnancy outcomes	all 858 twin pregnancies at 23+ weeks delivered at NYC Mt Sinai from June 2005 to December 2016	congenital anomalies or aneuploidy, twin–twin transfusion, monochorionic–monoamniotic twins	Mt Sinai medical records	preterm delivery, gestational age, cerclage, Cesarean delivery, birthweight, birthweight percentile, preeclampsia, gestational diabetes, intrauterine fetal demise	ns	stillbirth not mentioned
Tanner 2018[408]	To examine the impact of race/ethnicity as a risk factor for cervical insufficiency, PTB and NICU admission	34,173 women with a pregnancy that started any time in 2012 and continuous Kaiser Permanente Northern California (KPNC) region membership, and delivered within the KPNC system	multiples, abortions	Kaiser Permanente Northern California (KPNC) medical centers' electronic medical records	cervical insufficiency, PTB, NICU admission	ns	stillbirth not mentioned
Tolcher 2020[142]	To compare rates of preeclampsia among low- and high-risk women who received aspirin compared with placebo for preeclampsia prevention, stratifying by race/ethnicity	5,673 normotensive, nulliparous women and women with pregestational insulin-treated diabetes mellitus, chronic hypertension, multiple gestations, or history of preeclampsia, enrolled (in low-risk and high-risk RCTs, respectively) at 13-26 weeks and randomized to 60 mg aspirin daily or placebo, with documented ethnicity and race	ns	Maternal-Fetal Medicine Units (MFMU) Network	preeclampsia, gestational age, preterm delivery, placental abruption, small for gestational age (SGA), stillbirth, neonatal death	ns	*In this trial, the risk of stillbirth was significantly increased among NH black women who received aspirin for the prevention of preeclampsia in comparison to NH black women who received placebo (p=0.048).*
Yankauer 1950[152]	To examine relationships between residential segregation and fetal and infant deaths by race	433,206 live births and unknown number of fetal deaths in NYC, 1945-1947	County of Richmond births	Vital data on pregnancy and infant wastage	fetal wastage and infant death	ns	no abstract
Yankauer 1958[179]	To determine whether or not social action (decisions of the United States Supreme Court, expansion of the public housing program, and anti-discrimination legislation) has lowered fetal and infant mortality for non-white individuals	439,349 live births and unknown number of fetal deaths in NYC, 1953-1955	County of Richmond births	Vital data on pregnancy and infant wastage	fetal and infant death	ns	no abstract
Zelnik 1974[130]	To assess outcomes of first pregnancies to teenagers by marital status	4,611 women identified through national probability sample of females living in households or college	ns	retrospective data obtained in interviews	livebirth, stillbirth, miscarriage, abortion,	ns	no abstract

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
		dormitories in the continental U.S. and aged 15-19 years at time of birth in 1970			disposition of illegitimate first live birth		
Government reports, stillbirth data restricted to 20+ weeks, by author and year, n=9							
Gregory 2014[409]	To examine trends in spontaneous intrauterine deaths and perinatal mortality by race and Hispanic origin	Births in the 50 states, DC and selected territories, 2000-2012	ns	NVS data including 2000–2012 Fetal Death Data Files, 2006–2011 Linked Birth/Infant Death Data Sets, and 2000–2012 Birth Data Files	stillbirth, perinatal mortality	spontaneous intrauterine deaths at 20+ weeks	no abstract
MacDorman and Hoyert 2007[410]	To present national 2003 fetal and perinatal mortality data by a variety of characteristics (maternal age, marital status, race, Hispanic origin, state, birthweight, gestational age, plurality, sex)	all 4,115,660 infant deaths of <28 days of age and fetal deaths of 20+ weeks in the 50 U.S. states, DC, PR, USVI, and Guam, 2003	induced abortions; data from Oklahoma	NCHS vital statistics data files: the 2003 fetal death data file (with data from all Reports of Fetal Death filed in the 50 states, DC, PR, USVI, and Guam) and the 2003 period linked birth/infant death data file (data from death certificates is linked to data from birth certificates for each infant death <1 year)	fetal and perinatal mortality	fetal deaths of 20+ weeks	*Fetal mortality rates are higher for NH black women*
MacDorman and Munson 2007[411]	To present national 2004 data on fetal and perinatal deaths by maternal age, marital status, race, Hispanic origin, state, birthweight, gestational age, plurality, sex	4,137,710 infant deaths of <28 days of age and fetal deaths of 20+ weeks in the 50 states, DC, PR, USVI, and Guam, 2004	induced abortions; data from Oklahoma	NCHS vital statistics data files: the 2004 fetal death data file (with data from all Reports of Fetal Death filed in the 50 states, DC, PR, USVI, and Guam) and the 2004 period linked birth/infant death data file (data from death certificates is linked to data from birth certificates for each infant death <1 year)	fetal and perinatal mortality	fetal deaths of 20+ weeks	*The fetal mortality rate for NH black women (11.25) was 2.3 times the rate for NH white women (4.98), whereas the rate for Hispanic women (5.43) was 9 percent higher than the rate for NH white women*
MacDorman and Kirmeyer 2009a[135]	To examine fetal death data from the National Vital Statistics System	25,894 fetal deaths in the U.S., 2005	ns	fetal death data from the National Vital Statistics System (NVSS)	fetal death	fetal deaths of 20+ weeks	no abstract
MacDorman and Kirmeyer 2009b[412]	To present national 2005 data on fetal and perinatal deaths by maternal age, marital status, race, Hispanic origin, state, gestational age, birthweight, plurality, sex	4,164,467 infant deaths of <28 days of age and fetal deaths of 20+ weeks in the 50 states, DC, PR, USVI, and Guam, 2005	induced abortions	NCHS vital statistics data files: the 2005 fetal death data file (with data from all Reports of Fetal Death filed in the 50 states, DC, PR, USVI, and Guam) and the 2005 period linked birth/infant death data file (data from death certificates is linked to data from birth certificates for each infant death <1 year)	fetal death, perinatal death	fetal deaths of 20+ weeks	*From 2003 to 2005, fetal mortality rates declined significantly for NH white and NH black women, but not for Hispanic, American Indian or Alaska Native (AIAN), or Asian or Pacific Islander women. In 2005, the fetal mortality rate for NH black women (11.13) was 2.3 times the rate for NH white women (4.79), the rate for AIAN women (6.17) was 29% higher, and the rate for Hispanic women (5.44) was 14% higher*
MacDorman 2012[413]	To provide national 2006 data on fetal and perinatal deaths by maternal age, marital status, race, Hispanic origin, state, gestational age, birthweight, plurality, sex	4,291,565 infant deaths of <28 days of age and fetal deaths of 20+ weeks in the 50 states, DC, PR, USVI, and Guam, 2006	induced abortions	NCHS vital statistics data files: the 2006 fetal death data file (with data from all Reports of Fetal Death filed in the 50 states, DC, PR, USVI, and Guam) and the 2006 period linked birth/infant death data file (data from death certificates is linked to data from	fetal and perinatal death	fetal deaths of 20+ weeks	*Fetal mortality rates declined significantly for NH black women from 2005 to 2006 but not for other racial and ethnic groups. In 2006, the fetal mortality rate for NH black women (10.73) was more than twice the rate for NH white (4.81) and Asian or Pacific*

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
				birth certificates for each infant death <1 year)			*Islander (4.89) women. The rate for American Indian or Alaska Native women (6.04) was 26% higher, and the rate for Hispanic women (5.29) was 10% higher, than the rate for NH white women*
MacDorman 2015[2]	To present national 2013 data on fetal and perinatal deaths by maternal age, marital status, race, Hispanic origin, state, gestational age, birthweight, plurality, sex	3,955,776 infant deaths of <28 days of age and fetal deaths of 20+ weeks in the 50 US states, DC, American Samoa, Guam, the Northern Marianas, and PR, 2013	induced abortions	NCHS vital statistics data files: the 2013 fetal death data file (with data from all Reports of Fetal Death filed in the 50 states, DC, American Samoa, Guam, the Northern Marianas, and PR) and the 2013 period linked birth/infant death data file (data from death certificates is linked to data from birth certificates for each infant death <1 year)	fetal and perinatal death	fetal deaths of 20+ weeks	*In 2013, the fetal mortality rate for NH black women (10.53) was more than twice the rate for NH white (4.88) and Asian or Pacific Islander (4.68) women. The rate for American Indian or Alaska Native women (6.22) was 27% higher, and the rate for Hispanic women (5.22) was 7% higher, than the rate for NH white women*
Powell-Griner 1989[414]	To describe perinatal mortality in the United States	Fetal deaths, infant deaths, and live births to U.S. residents reported to NCHS, 1981-1985	New Jersey residents for race-disaggregated data; fetal deaths of not-stated gestation for states requiring reporting of all products of conception unless birthweight of 500+ g	NCHS data on fetal deaths, infant deaths, and live births	perinatal mortality	deaths of fetuses of 20+ weeks	*The perinatal mortality rate was higher for the black (17.4) than the white population (9.6). The race differential widened between 1981 and 1985 because the rate of decline for the white population (15%) exceeded that of the black population (10%)*
Pruitt 2020[189]	To analyze racial/ethnic disparities in fetal mortality	Fetal deaths and births in the U.S., 2015-2017	births to non-U.S. residents and <20 weeks' gestation	fetal death data files and birth certificates from NVSS	stillbirth	losses at 20+ weeks	no abstract
Government reports, stillbirth data not restricted to 20+ weeks, by author and year, n=6							
Barfield 2004[16]	To assess progress towards meeting the national goal of reducing fetal deaths to 4.1 per 1000 total births	all fetal deaths and live births in the U.S., 1990-2000	Oklahoma births, <20 weeks gestation	NVSS	stillbirth	involuntary fetal deaths of 20+ weeks (known or presumed)	no abstract
Hoyert 1996[150]	To present data for fetal death variation by education and use of prenatal care	19,966 births from 31 states, 1990	induced abortions; no data on Hispanic origin or <90% data complete; <80% complete data for education	NCHS	fetal death	stated or presumed period of gestation of 20+ weeks	*Fetal mortality for 1990 was higher for white mothers of all ages who had less schooling*
NCHS 1966[415]	To present national data on infant, fetal, and maternal deaths, including by cause of death, race, sex, and region	94,194 fetal deaths registered in the U.S. including those occurring to non-resident aliens, 1963	fetal deaths recorded in Boston for which data were unavailable; New Jersey residents (for race-disaggregated data)	National Center for Vital Statistics	infant and fetal death and maternal mortality	gestations of 20+ weeks or GA not stated	no abstract
Schlenker 2009[416]	To gain understanding of the decline in the Black IMR in Dane County, Wisconsin	97,590 birth, infant death, and fetal death records in Dane County, Wisconsin, 1990-2007	ns	Wisconsin Department of Health Services vital records including birth, death, and fetal death certificates	infant mortality, fetal mortality	any delivery of 20+ weeks or if fetus weighs 350+ g when death is indicated by the fetus	no abstract

Author and year	Aim	Population	Exclusions	Data source	Outcomes	Stillbirth definition	Relevant results are paraphrased from abstracts (see citations)
						showing no evidence of life	
Shapiro 1965[174]	To analyze trends in infant, fetal and perinatal mortality by age at death, cause of death, sex, color [sic], and geographic area, and the role of risk factors including birthweight, age of mother, birth order, and prior pregnancy loss	4,167,362 livebirths in the U.S. as well as fetal deaths of 20+ weeks (n not reported), 1942-1962	ns	official vital statistics, primarily the Division of Vital Statistics, Public Health Service; also vital statistics for upstate New York	infant, fetal, perinatal mortality	fetal deaths of 20+ weeks or GA unknown	no abstract
U.S. Dept of Commerce 1936[417]	To report national 1934 birth, stillbirth and infant mortality data	2,246,139 births in the continental U.S., Hawaii, and USVI, 1934	ns	birth, death, and stillbirth certificates	stillbirth, live births and infant mortality, also cause-specific stillbirth	varied (different definitions for each state, ranging from all products of conception in MD to 7th month in WA, ND and IN)	no abstract
Government reports, unknown whether stillbirth data restricted to 20+ weeks, n=1							
Koonin 1997[418]	To understand risk factors for pregnancy-related deaths	1,459 pregnancy-related deaths in the U.S., 1987-1990	pregnancy-related deaths in Puerto Rico; deaths related to ectopic pregnancy or abortion, deaths before delivery, time period between delivery and death >1 year	health departments in the 50 states, DC, NYC, and PR provided CDC with death certificates and available matched pregnancy-outcome records	pregnancy-related death	ns	no abstract

Abbreviations: AA, African American, ACOG, American College of Obstetricians and Gynecologists, AIAN, American Indian/Alaska Native, AP, antepartum, BMI, body mass index, CDC, Centers for Disease Control, CI, confidence interval, DOH, Dept of Health, FD, fetal death, GA, gestational age, GDM, gestational diabetes mellitus, HR, hazard ratio, HRR, Hospital Reference Regions, ICD, International Classification of Diseases, IDD, intellectual or developmental disability, IM, infant mortality, IMR, infant mortality rate, IP, intrapartum, IPI, interpregnancy interval, IUFD, intrauterine fetal demise, LBW, low birthweight, LGA, large for gestational age, LMP, last menstrual period, NCHS, National Center for Health Statistics, NH, non-Hispanic, NHB, non-Hispanic Black, NHW, non-Hispanic white, NICHD, National Institute of Child Health and Human Development, NICU, neonatal intensive care unit, NL, neonatal lupus, NND, neonatal death, ns, not stated, NVS, National Vital Statistics, NVSS, National Vital Statistics System, OR, odds ratio, PR, Puerto Rico, PRR, prevalence rate ratio, PTB, preterm birth, RCT, randomized controlled trial, ROR, relative odds ratios, RR, risk ratio, SB, stillbirth, SD, standard deviation, SGA, small for gestational age, SLE, systemic lupus erythematosus, USVI, U.S. Virgin Islands.

Table A9: Stillbirth definitions used in the 70 reports which provided any definition

Definition	# reports using this definition
>500 g	1
20+ weeks	36
20+ and >500 g	4
20+ and 500 g+	2
20+ and Apgar 0	1
20+ known or presumed	2
20+ or 350 g+	5
20+ or 500 g+	1
20+ or unknown	2
20+ presumed	1
21+	2
23+ and >400 g	1
23+ and ICD codes	1
24+	3
24+ and 500 g+	2
28+	1
Apgar 0 and no signs of life	1
ICD codes	4
TOTAL	70

Two reports allowed varied definitions of stillbirth and 23 provided no definition.

Table A10: Black-white Stillbirth Disparity Ratios (95% CIs) with exposures, factors stratified or modified by, and domains of analysis (n=1,143 SDRs from 83 reports)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
Akobirshoev 2019	OR for SB in women with IDD (NHW v NHB)	X					age, insurance, median household income for zip code, co-morbidities, hospital (location, teaching status, bed number, region), yr	2.50 (1.16, 5.38)
Allen 2005	OR for FD (B v W)	X					GA, age, PNC	1.1 (0.9, 1.3)
Ananth 2005	OR for FD (B v W)	X					gravidity, ed, marital, PNC, cohort, age, period	2.3 (2.1, 2.6)
	OR for SB in women with prior ID (1981-1985 v 1996-2000)	X	X				gravidity, mat ed, marital, and PNC	0.66
August 2011	HR for SB (B v W)	X					mat sociodem characs	2.06 (1.78, 2.39)
	HR for SB (prior ID v no ID)	X		X			sociodem variables, preg comp	2.18
	HR for SB (prior NND v no NND)	X		X				2.12
	HR for SB (post-NND v no post-NND)	X		X			"	2.77
	HR for SB (W or B with ID v W no ID)	X		X			sociodem variables	4.21
	HR for SB (W or B with NND v W no NND)	X		X			"	4.06
	HR for SB (W or B with post-NND v W no post-NND)	X		X			"	5.5
Barfield 1996	RR for FD in civilians (B v W)	X		X				1.69 (1.60, 1.78)
	RR for FD in military (B v W)	X		X				1.30 (1.02, 1.66)
Barfield 2004	# FDs per 1000 TB, NHW and NHB, 1990		X				n/a	2.17
	# FDs per 1000 TB, NHW and NHB, 1991		X				n/a	2.12
	# FDs per 1000 TB, NHW and NHB, 1992		X				n/a	2.17
	# FDs per 1000 TB, NHW and NHB, 1993		X				n/a	2.18
	# FDs per 1000 TB, NHW and NHB, 1994		X				n/a	2.16
	# FDs per 1000 TB, NHW and NHB, 1995		X				n/a	2.16
	# FDs per 1000 TB, NHW and NHB, 1996		X				n/a	2.11
	# FDs per 1000 TB, NHW and NHB, 1997		X				n/a	2.18
	# FDs per 1000 TB, NHW and NHB, 1998		X				n/a	2.2
	# FDs per 1000 TB, NHW and NHB, 1999		X				n/a	2.28
	# FDs per 1000 TB, NHW and NHB, 2000		X				n/a	2.28
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1990		X				n/a	2.63
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1991		X				n/a	2.54
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1992		X				n/a	2.64
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1993		X				n/a	2.68
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1994		X				n/a	2.54
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1995		X				n/a	2.62
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1996		X				n/a	2.54
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1997		X				n/a	2.68
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1998		X				n/a	2.64
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 1999		X				n/a	2.84
	# FDs per 1000 TB, NHW and NHB, 20-27 wk, 2000		X				n/a	2.72
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1990		X				n/a	1.83
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1991		X				n/a	1.79
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1992		X				n/a	1.82
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1993		X				n/a	1.75
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1994		X				n/a	1.81
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1995		X				n/a	1.77
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1996		X				n/a	1.71
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1997		X				n/a	1.77
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1998		X				n/a	1.79

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 1999		X				n/a	1.79
	# FDs per 1000 TB, NHW and NHB, 28+ wk, 2000		X				n/a	1.86
Brisendine 2020	OR for SB (NHW v NHB), 25-29 yr	X		X			parity, hyperten disorders, diab	2.42 (2.35, 2.48)
	OR for SB (NHW v NHB), <20 yr	X		X			"	1.74 (1.66, 1.82)
	OR for SB (NHW v NHB), 20-24 yr	X		X			"	1.93 (1.87, 1.99)
	OR for SB (NHW v NHB), 30-34 yr	X		X			"	2.64 (2.56, 2.73)
	OR for SB (NHW v NHB), 35-39 yr	X		X			"	2.32 (2.22, 2.42)
	OR for SB (NHW v NHB), 40+ yr	X		X			"	2.25 (2.10, 2.41)
	OR for SB (NHW v NHB), 20-27 wk 25-29 yr	X	X	X			"	2.86 (2.74, 2.99)
	OR for SB (NHW v NHB), 20-27 wk <20 yr	X	X	X			"	1.99 (1.85, 2.13)
	OR for SB (NHW v NHB), 20-27 wk 20-24 yr	X	X	X			"	2.14 (2.03, 2.26)
	OR for SB (NHW v NHB), 20-27 wk 30-34 yr	X	X	X			"	3.19 (3.02, 3.36)
	OR for SB (NHW v NHB), 20-27 wk 35-39 yr	X	X	X			"	2.60 (2.42, 2.78)
	OR for SB (NHW v NHB), 20-27 wk 40+ yr	X	X	X			"	2.62 (2.35, 2.94)
	OR for SB (NHW v NHB), 28+ wk 25-29 yr	X	X	X			"	2.19 (2.12, 2.26)
	OR for SB (NHW v NHB), 28+ wk <20 yr	X	X	X			"	1.59 (1.50, 1.68)
	OR for SB (NHW v NHB), 28+ wk 20-24 yr	X	X	X			"	1.82 (1.75, 1.89)
	OR for SB (NHW v NHB), 28+ wk 30-34 yr	X	X	X			"	2.35 (2.25, 2.45)
	OR for SB (NHW v NHB), 28+ wk 35-39 yr	X	X	X			"	2.15 (2.03, 2.27)
	OR for SB (NHW v NHB), 28+ wk 40+ yr	X	X	X			"	2.04 (1.87, 2.23)
	OR for SB (20-24 v <20 yr)	X		X			"	1.12
	OR for SB (25-29 v <20 yr)	X		X			"	1.41
	OR for SB (30-34 v <20 yr)	X		X			"	1.52
	OR for SB (35-39 v <20 yr)	X		X			"	1.34
	OR for SB (40+ v <20 yr)	X		X			"	1.29
	OR for 20-27 wk SB (20-24 v <20 yr)		X	X			"	1.10
	OR for 20-27 wk SB (25-29 v <20 yr)		X	X			"	1.50
	OR for 20-27 wk SB (30-34 v <20 yr)		X	X			"	1.69
	OR for 20-27 wk SB (35-39 v <20 yr)		X	X			"	1.38
	OR for 20-27 wk SB (40+ v <20 yr)		X	X			"	1.39
	OR for 28+ wk SB (20-24 v <20 yr)		X	X			"	1.13
	OR for 28+ wk SB (25-29 v <20 yr)		X	X			"	1.35
	OR for 28+ wk SB (30-34 v <20 yr)		X	X			"	1.43
	OR for 28+ wk SB (35-39 v <20 yr)		X	X			"	1.31
	OR for 28+ wk SB (40+ v <20 yr)		X	X			"	1.23
Brown 2007	OR for FD (AA v W)	X					age, residence, comorbidity, substance abuse, psychologic abnormality, length of hospital stay, total hospital charges	1.41 (0.90, 2.20)
Brown 2012	OR for SB (segregation, high v low)	X				X	age, marital, yr, county level (residential seg, median household income, % adults >25 with HS degree)	1.4
	OR for SB, low segregation counties (NHB v W)	X				X	"	1.67 (1.52, 1.83)
	OR for SB, high segregation counties (NHB v W)	X				X	"	2.35 (2.16, 2.55)
Buck 1995	# FDs per 1000 TB, W and B						n/a	1.63 (1.53, 1.73)
	# FDs per 1000 TB, W and B, 10-14 yrs			X			n/a	1.36 (0.54, 3.43)
	# FDs per 1000 TB, W and B, 15-19 yrs			X			n/a	1.30 (1.14, 1.50)
	# FDs per 1000 TB, W and B, 20-29 yrs			X			n/a	1.69 (1.56, 1.84)
	# FDs per 1000 TB, W and B, 30-44 yrs			X			n/a	1.68 (1.49, 1.90)
	# FDs per 1000 TB, W and B, 45+ yrs			X			n/a	4.04 (1.10, 14.83)
	# FDs per 1000 TB, W and B, mat cond			X			n/a	2.59 (1.89, 3.55)
	# FDs per 1000 TB, W and B, mat comp of preg			X			n/a	1.91 (1.68, 2.18)
	# FDs per 1000 TB, W and B, comp of placenta, cord, membranes			X			n/a	1.42 (1.25, 1.61)
	# FDs per 1000 TB, W and B, slow fetal growth and fetal maturation		X				n/a	0.77 (0.36, 1.66)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1000 TB, W and B, disorders relating to short gestation and unspecified LBW		X				n/a	2.79 (2.19, 3.56)
	# FDs per 1000 TB, W and B, intrauterine hypoxia and birth asphyxia		X				n/a	1.04 (0.73, 1.49)
	# FDs per 1000 TB, W and B, other respiratory cond of fetus		X				n/a	1.93 (0.94, 3.96)
	# FDs per 1000 TB, W and B, other and ill-defined cond originating in perinatal period			X			n/a	1.66 (1.50, 1.83)
	# FDs per 1000 TB, W and B, other			X			n/a	0.99 (0.76, 1.30)
Cai, Hoff and Archer 2007	# FDs over TB per 1000, W and B						n/a	2.08 (1.51, 2.85)
	# FDs over TB per 1000, W and B, Kansas City 500-1499g		X	X			n/a	2.25 (1.11, 4.56)
	# FDs over TB per 1000, W and B, Kansas City 1500-2499g		X	X			n/a	3.24 (1.10, 9.51)
	# FDs over TB per 1000, W and B, Kansas City 2500+g		X	X			n/a	3.24 (1.10, 9.51)
	# FDs over TB per 1000, W and B, Balance of Jackson Cty, 500-1499g		X	X			n/a	1.90 (0.72, 5.02)
	# FDs over TB per 1000, W and B, Balance of Jackson Cty, 1500-2499g		X	X			n/a	0.52 (0.07, 3.95)
	# FDs over TB per 1000, W and B, Balance of Jackson Cty, 2500+g		X	X			n/a	1.48 (0.43, 5.04)
Cai, Hoff and Okah 2007	RaR for FM (NHB v NHW)	X					unadjusted	2.30 (1.93, 2.70)
	RaR for FM (NHB v NHW), 20-27 wk	X	X				unadjusted	0.60 (0.56, 0.84)
	RaR for FM (NHB v NHW), 28+ wk	X	X				unadjusted	2.20 (1.71, 2.70)
	RaR for FM (NHB v NHW), <2500 g	X	X				unadjusted	1.20 (0.99, 1.43)
	RaR for FM (NHB v NHW), 2500+ g	X	X				unadjusted	1.70 (1.11, 2.35)
Carmichael 2015	RR for SB (1 BMI unit increase), multips 37-41 wk	X	X	X			age, ed, height	1.04
	RR for SB (5 BMI unit increase), multips 37-41 wk	X	X	X			"	1.17
	RR for SB (10 BMI unit increase), multips 37-41 wk	X	X	X			"	1.19
	RR for SB (15 BMI unit increase), multips 37-41 wk	X	X	X			"	1.04
	RR for SB (20 BMI unit increase), multips 37-41 wk	X	X	X			"	0.79
	RR for SB (1 BMI unit increase), multips 32-36 wk	X	X	X			"	0.98
	RR for SB (5 BMI unit increase), multips 32-36 wk	X	X	X			"	0.94
	RR for SB (10 BMI unit increase), multips 32-36 wk	X	X	X			"	0.89
	RR for SB (15 BMI unit increase), multips 32-36 wk	X	X	X			"	0.83
	RR for SB (20 BMI unit increase), multips 32-36 wk	X	X	X			"	0.79
	RR for SB (1 BMI unit increase),multips 28-31 wk	X	X	X			"	0.96
	RR for SB (5 BMI unit increase), multips 28-31 wk	X	X	X			"	0.81
	RR for SB (10 BMI unit increase), multips 28-31 wk	X	X	X			"	0.66
	RR for SB (15 BMI unit increase), multips 28-31 wk	X	X	X			"	0.54
	RR for SB (20 BMI unit increase), multips 28-31 wk	X	X	X			"	0.44
	RR for SB (1 BMI unit increase), multips 24-27 wk	X	X	X			"	0.95
	RR for SB (5 BMI unit increase), multips 24-27 wk	X	X	X			"	0.79
	RR for SB (10 BMI unit increase), multips 24-27 wk	X	X	X			"	0.62
	RR for SB (15 BMI unit increase), multips 24-27 wk	X	X	X			"	0.49
	RR for SB (20 BMI unit increase), multips 24-27 wk	X	X	X			"	0.38
	RR for SB (1 BMI unit increase), multips 20-23 wk	X	X	X			"	1.00
	RR for SB (5 BMI unit increase), multips 20-23 wk	X	X	X			"	0.99
	RR for SB (10 BMI unit increase), multips 20-23 wk	X	X	X			"	0.99
	RR for SB (15 BMI unit increase), multips 20-23 wk	X	X	X			"	0.99
	RR for SB (20 BMI unit increase), multips 20-23 wk	X	X	X			"	0.99
	RR for SB (1 BMI unit increase), nullips 37-41 wk	X	X	X			"	0.93
	RR for SB (5 BMI unit increase), nullips 37-41 wk	X	X	X			"	0.75
	RR for SB (10 BMI unit increase), nullips 37-41 wk	X	X	X			"	0.66
	RR for SB (15 BMI unit increase), nullips 37-41 wk	X	X	X			"	0.67
	RR for SB (20 BMI unit increase), nullips 37-41 wk	X	X	X			"	0.79
	RR for SB (1 BMI unit increase), nullips 32-36 wk	X	X	X			"	1.01
	RR for SB (5 BMI unit increase), nullips 32-36 wk	X	X	X			"	1.10

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	RR for SB (10 BMI unit increase), nullips 32-36 wk	X	X	X			"	1.19
	RR for SB (15 BMI unit increase), nullips 32-36 wk	X	X	X			"	1.30
	RR for SB (20 BMI unit increase), nullips 32-36 wk	X	X	X			"	1.42
	RR for SB (1 BMI unit increase), nullips 28-31 wk	X	X	X			"	0.98
	RR for SB (5 BMI unit increase), nullips 28-31 wk	X	X	X			"	0.93
	RR for SB (10 BMI unit increase), nullips 28-31 wk	X	X	X			"	0.86
	RR for SB (15 BMI unit increase), nullips 28-31 wk	X	X	X			"	0.80
	RR for SB (20 BMI unit increase), nullips 28-31 wk	X	X	X			"	0.74
	RR for SB (1 BMI unit increase), nullips 24-27 wk	X	X	X			"	0.97
	RR for SB (5 BMI unit increase), nullips 24-27 wk	X	X	X			"	0.89
	RR for SB (10 BMI unit increase), nullips 24-27 wk	X	X	X			"	0.80
	RR for SB (15 BMI unit increase), nullips 24-27 wk	X	X	X			"	0.71
	RR for SB (20 BMI unit increase), nullips 24-27 wk	X	X	X			"	0.64
	RR for SB (1 BMI unit increase), nullips 20-23 wk	X	X	X			"	0.98
	RR for SB (5 BMI unit increase), nullips 20-23 wk	X	X	X			"	0.90
	RR for SB (10 BMI unit increase), nullips 20-23 wk	X	X	X			"	0.81
	RR for SB (15 BMI unit increase), nullips 20-23 wk	X	X	X			"	0.72
	RR for SB (20 BMI unit increase), nullips 20-23 wk	X	X	X			"	0.65
	RR for SB (overweight v normal), multips 37-41 wk	X	X	X			"	0.52
	RR for SB (class 1 obese v normal), multips 37-41 wk	X	X	X			"	1.58
	RR for SB (overweight v normal), multips 32-36 wk	X	X	X			"	1.09
	RR for SB (class 1 obese v normal), multips 32-36 wk	X	X	X			"	1.79
	RR for SB (class 2 obese v normal), multips 32-36 wk	X	X	X			"	0.28
	RR for SB (class 3 obese v normal), multips 32-36 wk	X	X	X			"	1.16
	RR for SB (overweight v normal), multips 28-31 wk	X	X	X			"	0.72
	RR for SB (class 1 obese v normal), multips 28-31 wk	X	X	X			"	0.50
	RR for SB (class 2 obese v normal), multips 28-31 wk	X	X	X			"	0.66
	RR for SB (overweight v normal), multips 24-27 wk	X	X	X			"	1.06
	RR for SB (class 1 obese v normal), multips 24-27 wk	X	X	X			"	0.82
	RR for SB (class 2 obese v normal), multips 24-27 wk	X	X	X			"	1.13
	RR for SB (overweight v normal), multips 20-23 wk	X	X	X			"	0.89
	RR for SB (class 1 obese v normal), multips 20-23 wk	X	X	X			"	1.08
	RR for SB (class 2 obese v normal), multips 20-23 wk	X	X	X			"	1.07
	RR for SB (class 3 obese v normal), multips 20-23 wk	X	X	X			"	0.98
	RR for SB (overweight v normal), nullips 37-41 wk	X	X	X			"	0.82
	RR for SB (class 1 obese v normal), nullips 37-41 wk	X	X	X			"	0.53
	RR for SB (class 3 obese v normal), nullips 37-41 wk	X	X	X			"	0.98
	RR for SB (overweight v normal), nullips 32-36 wk	X	X	X			"	1.67
	RR for SB (class 1 obese v normal), nullips 32-36 wk	X	X	X			"	0.95
	RR for SB (overweight v normal), nullips 28-31 wk	X	X	X			"	0.74
	RR for SB (class 1 obese v normal), nullips 28-31 wk	X	X	X			"	0.33
	RR for SB (overweight v normal), nullips 24-27 wk	X	X	X			"	0.88
	RR for SB (class 1 obese v normal), nullips 24-27 wk	X	X	X			"	1.28
	RR for SB (class 2 obese v normal), nullips 24-27 wk	X	X	X			"	1.63
	RR for SB (overweight v normal), nullips 20-23 wk	X	X	X			"	1.19
	RR for SB (class 1 obese v normal), nullips 20-23 wk	X	X	X			"	0.73
	RR for SB (class 2 obese v normal), nullips 20-23 wk	X	X	X			"	1.43
	RR for SB (class 3 obese v normal), nullips 20-23 wk	X	X	X			"	0.53
Carmichael 2019	OR for SB (NHB v NHW singleton full-term livebirth), 20-25 wk	X					ed, payer, country of birth, BMI, smoking, pre-preg diab and hyperten, parity, IPI, prior SB or PTB	2.03 (1.79, 2.29)
	PR for SB (NHB v NHW), 20-21 wk	X	X				unadjusted	2.51 (2.16, 2.92)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	PR for SB (NHB v NHW), 22-23 wk	X	X				unadjusted	2.29 (1.95, 2.70)
	PR for SB (NHB v NHW), 24-25 wk	X	X				unadjusted	2.62 (2.10, 3.27)
	PR for SB (NHB v NHW), 20-25 wk	X	X				unadjusted	2.45 (2.22, 2.70)
Clowse 2016	OR for SB in mothers with SLE (B v W)	X					age, insurance, thrombophilia, anemia, thrombocytopenia, drug use, alcohol use, tobacco use, chronic hyperten, chronic renal failure, diab, thyroid disorders, asthma, history of myocardial infarction, plurality, mode of delivery, placenta previa	1.61 (1.15, 2.25)
Creanga 2017	% preg-related deaths						n/a	0.74 (0.47, 1.15)
Demissie 2001	# FDs per 1000 TB, W and B, 1997		X				n/a	1.74 (1.67, 1.81)
	# FDs per 1000 TB, W and B, 1989		X				n/a	1.71 (1.65, 1.77)
Dryfhout 2010	OR for SB (B v W full-term)	X					smoking, physical activity, plurality, mat weight, cramps, bleeding, age, parity, marital, income, ed, occupation, insurance, PNC provider, trimester at PNC initiation, # PNC visits	1.69
Dumas 2020	# non-LB per 1,000 subjects, W and B						n/a	0.84 (0.66, 1.06)
Faiz 2012	HR for SB (NHB v NHW)	X					mat characs, preg comp	1.90 (1.70, 2.10)
Getahun 2005	RR for SB (both parents B v W)	X					age, ed, paternal age, PNC, parity, marital, smoking	1.67 (1.62, 1.72)
Getahun 2007	HR for AP SB (35+ v 20-24)	X	X	X			ed, marital, parity, PNC, BMI, smoking, sex, prior PTB or SGA, current SGA, COD, gest weight gain	0.8
	HR for AP SB (<20 v 20-24)	X	X	X			"	0.78
	HR for AP SB (25-29 v 20-24)	X	X	X			"	1.00
	HR for AP SB (30-34 v 20-24)	X	X	X			"	0.91
	HR for AP SB <20 yr (NHAA v NHW)	X	X	X			"	1.3 (0.9, 1.7)
	HR for AP SB, 20-24 yr (NHAA v NHW)	X	X	X			"	1.2 (1.0, 1.6)
	HR for AP SB, 25-29 yr (NHAA v NHW)	X	X	X			"	1.5 (1.1, 1.9)
	HR for AP SB, 30-34 yr (NHAA v NHW)	X	X	X			"	1.3 (0.9, 1.8)
	HR for AP SB, 35+ yr (NHAA v NHW)	X	X	X			"	1.1 (0.7, 1.0)
	HR for IP SB (35+ v 20-24)	X	X	X			"	0.89
	HR for IP SB (<20 v 20-24)	X	X	X			"	1.50
	HR for IP SB (25-29 v 20-24)	X	X	X			"	0.75
	HR for IP SB (30-34 v 20-24)	X	X	X			"	1.17
	HR for IP SB, <20 yr (NHAA v NHW)	X	X	X			"	1.4 (0.7, 3.6)
	HR for IP SB, 20-24 yr (NHAA v NHW)	X	X	X			"	0.9 (0.5, 1.6)
	HR for IP SB, 25-29 yr (NHAA v NHW)	X	X	X			"	0.9 (0.4, 2.2)
	HR for IP SB, 30-34 yr (NHAA v NHW)	X	X	X			"	1.0 (0.4, 2.8)
	HR for IP SB, 35+ yr (NHAA v NHW)	X	X	X			"	1.5 (0.5, 4.5)
	HR for AP SB (<8 v 12+ yrs ed)	X	X	X			"	0.96
	HR for AP SB (8-11 v 12+ yrs ed)	X	X	X			"	0.92
	HR for AP SB , <8 yr ed (NHAA v NHW)	X	X	X			"	1.4 (1.0, 2.1)
	HR for AP SB, 8-11 yr ed (NHAA v NHW)	X	X	X			"	1.2 (0.9, 1.5)
	HR for AP SB, 12+ yr ed (NHAA v NHW)	X	X	X			"	1.3 (1.1, 1.5)
	HR for IP SB (<8 v 12+ yrs ed)	X	X	X			"	1.53
	HR for IP SB (8-11 v 12+ yrs ed)	X	X	X			"	0.93
	HR for IP SB, <8 yr ed (NHAA v NHW)	X	X	X			"	1.8 (0.5, 5.2)
	HR for IP SB, 8-11 yr ed (NHAA v NHW)	X	X	X			"	1.2 (0.6, 2.4)
	HR for IP SB, 12+ yr ed (NHAA v NHW)	X	X	X			"	0.9 (0.6, 1.4)
	HR for AP SB (unmarried v married)	X	X	X			"	0.90
	HR for AP SB, unmarried	X	X	X			"	1.2 (1.0, 1.4)
	HR for IP SB (unmarried v married)	X	X	X			"	0.53
	HR for IP SB, unmarried (NHAA v NHW)	X	X	X			"	0.9 (0.6, 1.4)
	HR for AP SB (multi v nulli)	X	X	X			"	1.15

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	HR for AP SB, multiparous (NHAA v NHW)	X	X	X			"	1.3 (1.1, 1.5)
	HR for AP SB, nullips (NHAA v NHW)	X	X	X			"	1.2 (0.9, 1.5)
	HR for IP SB (multi v nulli)	X	X	X			"	0.50
	HR for IP SB, multiparous (NHAA v NHW)	X	X	X			"	1.1 (0.8, 1.7)
	HR for IP SB, nullips (NHAA v NHW)	X	X	X			"	0.8 (0.4, 1.7)
	HR for AP SB (late/no vs on-time PNC)	X	X		X		"	0.77
	HR for AP SB, late/no PNC (NHAA v NHW)	X	X		X		"	1.0 (0.8, 1.3)
	HR for IP SB (late/no vs on-time PNC)	X	X		X		"	0.64
	HR for IP SB, late/no PNC (NHAA v NHW)	X	X		X		"	0.8 (0.4, 1.7)
	HR for AP SB (<18.5 v 18.5-25 BMI)	X	X	X			"	2.00
	HR for AP SB (25-30 v 18.5-25 BMI)	X	X	X			"	1.00
	HR for AP SB (30+ v 18.5-25 BMI)	X	X	X			"	0.92
	HR for AP SB, <18.5 BMI (NHAA v NHW)	X	X	X			"	1.6 (1.2, 2.2)
	HR for AP SB, 18.5-25 BMI (NHAA v NHW)	X	X	X			"	1.2 (1.0, 1.4)
	HR for AP SB, 25-30 BMI (NHAA v NHW)	X	X	X			"	1.1 (0.8, 1.5)
	HR for AP SB, 30+ BMI (NHAA v NHW)	X	X	X			"	1.2 (0.9, 1.7)
	HR for IP SB (<18.5 v 18.5-25 BMI)	X	X	X			"	1.90
	HR for IP SB (25-30 v 18.5-25 BMI)	X	X	X			"	0.80
	HR for IP SBI (30+ v 18.5-25 BMI)	X	X	X			"	1.57
	HR for IP SB, <18.5 BMI (NHAA v NHW)	X	X	X			"	1.6 (0.8, 3.4)
	HR for IP SB, 18.5-25 BMI (NHAA v NHW)	X	X	X			"	1.0 (0.6, 1.6)
	HR for IP SB, 25-30 BMI (NHAA v NHW)	X	X	X			"	0.7 (0.3, 1.7)
	HR for IP SB, 30+ BMI (NHAA v NHW)	X	X	X			"	1.4 (0.6, 3.6)
	HR for AP SB (excess gain v not)	X	X	X			"	0.67
	HR for AP SB, excess weight gain (NHAA v NHW)	X	X	X			"	0.9 (0.5, 1.3)
	HR for IP SB (excess gain v not)	X	X	X			"	0.60
	HR for IP SB, excess weight gain (NHAA v NHW)	X	X	X			"	0.5 (0.1, 2.4)
	HR for AP SB (smoking v not)	X	X	X			"	1.10
	HR for AP SB in smokers (NHAA v NHW)	X	X	X			"	1.2 (1.0, 1.6)
	HR for IP SB (smoking v not)	X	X	X			"	2.29
	HR for IP SB in smokers (NHAA v NHW)	X	X	X			"	2.1 (1.1, 4.3)
	HR for AP SB (M v F)	X	X				"	1.10
	HR for AP SB, males (NHAA v NHW)	X	X				"	1.3 (1.1, 1.6)
	HR for IP SB (M v F)	X	X				"	1.09
	HR for IP SB, males (NHAA v NHW)	X	X				"	1.1 (0.7, 1.7)
	HR for AP SB (prior SGA/PTB v not)	X	X	X			"	0.69
	HR for AP SB with prior SGA/PTB (NHAA v NHW)	X	X	X			"	1.1 (0.5, 2.4)
	HR for IP SB (prior SGA/PTB v not)	X	X	X			"	1.14
	HR for IP SB with prior SGA/PTB (NHAA v NHW)	X	X	X			"	1.5 (0.3, 8.4)
	HR for AP SB (SGA <5th centile v not)	X	X				"	0.77
	HR for AP SB, <5th centile (NHAA v NHW)	X	X				"	0.8 (0.6, 1.0)
	HR for AP SB (SGA <10th centile v not)	X	X				"	0.53
	HR for AP SB, <10th centile (NHAA v NHW)	X	X				"	0.9 (0.7, 1.1)
	HR for IP SB (SGA <5th centile v not)	X	X				"	4.75
	HR for IP SB, <5th centile (NHAA v NHW)	X	X				"	3.4 (1.5, 7.7)
	HR for IP SB (SGA <10th centile v not)	X	X				"	0.26
	HR for IP SB, <10th centile (NHAA v NHW)	X	X				"	1.5 (0.7, 2.9)
	HR for AP SB (CA v not)	X	X				"	0.83
	HR for AP SB with any congenital anomaly (NHAA v NHW)	X	X				"	1.0 (0.7, 1.6)
	HR for IP SB (CA v not)	X	X				"	1.17
	HR for IP SB with any congenital anomaly (NHAA v NHW)	X	X				"	1.1 (0.5, 2.3)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	HR for AP SB, (diab v not)	X	X	X			"	1.00
	HR for AP SB with diab (NHAA v NHW)	X	X	X			"	1.5 (0.8, 3.1)
	HR for IP SB (diab v not)	X	X	X			"	1.00
	HR for IP SB with diab (NHAA v NHW)	X	X	X			"	0.8 (0.1, 8.2)
	HR for AP SB (chronic hypert v not)	X	X	X			"	1.42
	HR for AP SB with chronic hypert (NHAA v NHW)	X	X	X			"	1.9 (0.9, 4.1)
	HR for IP SB (chronic hypert v not)	X	X	X			"	1.36
	HR for IP SB with chronic hypert (NHAA v NHW)	X	X	X			"	1.3 (0.1, 30.5)
	HR for AP SB (preg induced hypert v not)	X	X	X			"	1.71
	HR for AP SB with preg induced hypert (NHAA v NHW)	X	X	X			"	1.9 (1.2, 3.0)
	HR for IP SB (preg induced hypert v not)	X	X	X			"	0.43
	HR for IP SB with preg induced hypert (NHAA v NHW)	X	X	X			"	1.1 (0.1, 11.0)
	HR for AP SB (PROM no fever v no PROM no fever)	X	X	X			"	1.60
	HR for AP SB with PROM but no fever (NHAA v NHW)	X	X	X			"	1.7 (1.0, 3.2)
	HR for IP SB (PROM no fever v no PROM no fever)	X	X	X			"	1.56
	HR for IP SB with PROM but no fever (NHAA v NHW)	X	X	X			"	1.2 (0.6, 2.6)
	HR for AP SB (fever but no PROM v no PROM, no fever)	X	X	X			"	0.83
	HR for AP SB with fever but no PROM (NHAA v NHW)	X	X	X			"	1.3 (0.6, 2.9)
	HR for IP SB (fever but no PROM v no PROM, no fever)	X	X	X			"	1.94
	HR for IP SB with fever but no PROM (NHAA v NHW)	X	X	X			"	1.8 (0.3, 10.1)
	HR for AP SB (PROM and fever v no PROM or fever)	X	X	X			"	3.6
	HR for AP SB with PROM and fever (NHAA v NHW)	X	X	X			"	16.1 (1.9, 135.9)
	HR for IP SB (PROM and fever v no PROM or fever)	X	X	X			"	0.61
	HR for IP SB with PROM and fever (NHAA v NHW)	X	X	X			"	0.5 (0.1, 3.1)
	HR for AP SB (placental abruption v no)	X	X	X			"	1.07
	HR for AP SB with placental abruption (NHAA v NHW)	X	X	X			"	1.5 (1.1, 2.1)
	HR for IP SB (placental abruption v no)	X	X	X			"	2.44
	HR for IP SB with placental abruption (NHAA v NHW)	X	X	X			"	1.3 (0.7, 2.7)
	HR for AP SB (placenta previa v no)	X	X	X			"	0.27
	HR for AP SB with placenta previa (NHAA v NHW)	X	X	X			"	0.2 (0.0, 2.3)
	HR for AP SB (excessive bleeding v no)	X	X	X			"	1.69
	HR for AP SB with excessive bleeding (NHAA v NHW)	X	X	X			"	1.8 (0.9, 3.6)
	HR for AP SB (renal disease v no)	X	X	X			"	1.67
	HR for AP SB with renal disease (NHAA v NHW)	X	X	X			"	3.8 (0.4, 33.7)
	HR for AP SB (fetal distress v not)	X	X	X			"	1.00
	HR for AP SB with fetal distress (NHAA v NHW)	X	X				"	0.5 (0.2, 1.6)
	HR for IP SB (fetal distress v not)	X	X				"	1.75
	HR for IP SB with fetal distress (NHAA v NHW)	X	X				"	1.6 (0.7, 3.8)
	HR for AP SB (cord comp v not)	X	X				"	0.74
	HR for AP SB with cord comp (NHAA v NHW)	X	X				"	0.9 (0.4, 2.0)
	HR for IP SB (cord comp v not)	X	X				"	0.61
	HR for IP SB with cord comp (NHAA v NHW)	X	X				"	0.7 (0.2, 2.9)
	HR for AP SB (any one mat or fetal condition vs none)	X	X	X			"	0.90
	HR for AP SB with any one mat or fetal condition (NHAA v NHW)	X	X	X			"	1.4 (1.1, 1.7)
	HR for IP SB (any one mat or fetal condition vs none)	X	X	X			"	0.36
	HR for IP SB with any one mat or fetal condition (NHAA v NHW)	X	X	X			"	1.4 (1.0, 1.7)
Gold 2010	OR for SB (both parents B v W)	X					birthweight, GA, demographic factors, social, biological, and genetic/congenital risk factors, procedures	1.04 (0.86, 1.27)
Gould 2003	# FDs per 1000 TB, US-born NHW and NHB						n/a	1.82 (1.67, 1.98)
Grant 2017	% twin pregnancies that included any FDs, NHW and NHB						n/a	3.61 (1.17, 11.21)
Gregory 2003	RR for intrauterine fetal distress (35+ v <35)	X		X			unadjusted	1.38

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
Gregory 2014	# FDs per 1000 TB, NHW and NHB, late fetal 2006		X				n/a	1.88
	# FDs per 1000 TB, NHW and NHB, late fetal 2011		X				n/a	1.78
Guendelman 1994	OR for FD (NHW or NHB with prior FD v NHW with no prior FD)	X		X			unclear	2.4
Healy 2006	OR for FD 24+ wk (B v W)	X	X				age, ed, marital, BMI, smoking, drug use, alcohol use, medication during preg, pregest diab, obstetric history (prior live birth, miscarriage, PTB), ART, antihyperten med use prior to preg, site	3.10 (1.50, 6.20)
	OR for FD <24 wk (B v W)	X	X				"	3.2 (2.2, 4.8)
Hoyert 1996	# FDs per 1,000 TB, NHW and NHB						n/a	1.98 (1.88, 2.00)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs			X			n/a	1.50 (1.40, 1.61)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs			X			n/a	2.07 (2.00, 2.15)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs			X			n/a	2.13 (1.93, 2.35)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs of ed			X			n/a	1.71 (1.62, 1.81)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, <12 yrs ed			X			n/a	1.47 (1.35, 1.61)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, <12 yrs ed			X			n/a	1.95 (1.80, 2.11)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, <12 yrs ed			X			n/a	1.67 (1.32, 2.11)
	# FDs per 1,000 TB, NHW and NHB, 0-8 yrs of ed			X			n/a	1.96 (1.70, 2.26)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 0-8 yrs ed			X			n/a	1.88 (1.51, 2.33)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 0-8 yrs ed			X			n/a	2.31 (1.83, 2.90)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 0-8 yrs ed			X			n/a	1.73 (1.13, 2.65)
	# FDs per 1,000 TB, NHW and NHB, 9-11 yrs of ed			X			n/a	1.71 (1.60, 1.82)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 9-11 yrs ed			X			n/a	1.41 (1.28, 1.55)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 9-11 yrs ed			X			n/a	1.95 (1.79, 2.13)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 9-11 yrs ed			X			n/a	1.83 (1.35, 2.49)
	# FDs per 1,000 TB, NHW and NHB, 12+ yrs of ed			X			n/a	2.03 (1.96, 2.11)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 12+ yrs ed			X			n/a	1.56 (1.38, 1.75)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 12+ yrs ed			X			n/a	2.09 (2.01, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 12+ yrs ed			X			n/a	2.20 (1.98, 2.46)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs of ed			X			n/a	1.89 (1.81, 1.98)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 12 yrs ed			X			n/a	1.51 (1.34, 1.72)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 12 yrs ed			X			n/a	1.98 (1.88, 2.09)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 12 yrs ed			X			n/a	2.05 (1.76, 2.38)
	# FDs per 1,000 TB, NHW and NHB, 13-15 yrs of ed			X			n/a	1.98 (1.85, 2.13)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 13-15 yrs ed			X			n/a	2.04 (1.45, 2.87)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 13-15 yrs ed			X			n/a	1.98 (1.83, 2.14)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 13-15 yrs ed			X			n/a	2.16 (1.77, 2.65)
	# FDs per 1,000 TB, NHW and NHB, 16+ yrs of ed			X			n/a	2.30 (2.06, 2.57)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 16+ yrs ed			X			n/a	2.48 (2.19, 2.80)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 16+ yrs ed			X			n/a	1.84 (1.43, 2.36)
	# FDs per 1,000 TB, NHW and NHB, married			X			n/a	1.84 (1.73, 1.96)
	# FDs per 1,000 TB, NHW and NHB, unmarried			X			n/a	2.04 (1.90, 2.19)
	# FDs per 1,000 TB, NHW and NHB, married, <12 yrs ed			X			n/a	1.40 (1.14, 1.73)
	# FDs per 1,000 TB, NHW and NHB, unmarried, <12 yrs ed			X			n/a	1.81 (1.59, 2.06)
	# FDs per 1,000 TB, NHW and NHB, married, 0-8 yrs ed			X			n/a	1.62 (1.08, 2.42)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 0-8 yrs ed			X			n/a	2.86 (2.10, 3.90)
	# FDs per 1,000 TB, NHW and NHB, married, 9-11 yrs ed			X			n/a	1.39 (1.09, 1.78)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 9-11 yrs ed			X			n/a	1.66 (1.43, 1.93)
	# FDs per 1,000 TB, NHW and NHB, married, 12+ yrs ed			X			n/a	1.88 (1.76, 2.01)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 12+ yrs ed			X			n/a	1.74 (1.61, 1.89)
	# FDs per 1,000 TB, NHW and NHB, married, 12 yrs ed			X			n/a	2.02 (1.83, 2.22)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 12 yrs ed			X			n/a	1.67 (1.50, 1.85)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, married, 13-15 yrs ed			X			n/a	1.69 (1.50, 1.91)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 13-15 yrs ed			X			n/a	1.64 (1.40, 1.94)
	# FDs per 1,000 TB, NHW and NHB, married, 16+ yrs ed			X			n/a	1.89 (1.64, 2.18)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 16+ yrs ed			X			n/a	2.63 (2.01, 3.46)
	# FDs per 1,000 TB, NHW and NHB, met counties			X			n/a	2.25 (2.15, 2.36)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties			X			n/a	2.25 (2.01, 2.51)
	# FDs per 1,000 TB, NHW and NHB, met counties, <12 yrs ed			X			n/a	1.93 (1.73, 2.16)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties, <12 yrs ed			X			n/a	1.79 (1.39, 2.30)
	# FDs per 1,000 TB, NHW and NHB, met counties, 0-8 yrs ed			X			n/a	2.04 (1.57, 2.65)
	# FDs per 1,000 TB, NHW and NHB, met counties, 9-11 yrs ed			X			n/a	2.00 (1.75, 2.28)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties, 9-11 yrs ed			X			n/a	1.66 (1.25, 2.21)
	# FDs per 1,000 TB, NHW and NHB, met counties, 12+ yrs ed			X			n/a	2.30 (2.19, 2.42)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties, 12+ yrs ed			X			n/a	2.31 (2.04, 2.61)
	# FDs per 1,000 TB, NHW and NHB, met counties, 12 yrs ed			X			n/a	2.26 (2.11, 2.42)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties 12 yrs ed			X			n/a	2.22 (1.90, 2.60)
	# FDs per 1,000 TB, NHW and NHB, met counties, 13-15 yrs ed			X			n/a	2.11 (1.92, 2.32)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties, 13-15 yrs ed			X			n/a	1.93 (1.48, 2.52)
	# FDs per 1,000 TB, NHW and NHB, met counties, 16+ yrs ed			X			n/a	2.28 (2.02, 2.58)
	# FDs per 1,000 TB, NHW and NHB, nonmet counties, 16+ yrs ed			X			n/a	3.09 (2.22, 4.32)
	# FDs per 1,000 TB, NHW and NHB, birth order-1			X			n/a	2.53 (2.29, 2.81)
	# FDs per 1,000 TB, NHW and NHB, birth order-2			X			n/a	2.18 (1.99, 2.39)
	# FDs per 1,000 TB, NHW and NHB, birth order-3			X			n/a	2.11 (1.92, 2.31)
	# FDs per 1,000 TB, NHW and NHB, birth order-4			X			n/a	2.09 (1.88, 2.33)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+			X			n/a	1.71 (1.58, 1.87)
	# FDs per 1,000 TB, NHW and NHB, birth order-1, <12 yrs ed			X			n/a	1.97 (1.39, 2.79)
	# FDs per 1,000 TB, NHW and NHB, birth order-2, <12 yrs ed			X			n/a	1.89 (1.40, 2.56)
	# FDs per 1,000 TB, NHW and NHB, birth order-3, <12 yrs ed			X			n/a	2.48 (1.94, 3.17)
	# FDs per 1,000 TB, NHW and NHB, birth order-4, <12 yrs ed			X			n/a	1.90 (1.49, 2.42)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+, <12 yrs ed			X			n/a	1.54 (1.33, 1.80)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+, 0-8 yrs ed			X			n/a	1.63 (1.12, 2.36)
	# FDs per 1,000 TB, NHW and NHB, birth order-1, 9-11 yrs ed			X			n/a	1.81 (1.20, 2.74)
	# FDs per 1,000 TB, NHW and NHB, birth order-2, 9-11 yrs ed			X			n/a	1.78 (1.26, 2.52)
	# FDs per 1,000 TB, NHW and NHB, birth order-3, 9-11 yrs ed			X			n/a	2.19 (1.66, 2.89)
	# FDs per 1,000 TB, NHW and NHB, birth order-4, 9-11 yrs ed			X			n/a	2.07 (1.55, 2.74)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+, 9-11 yrs ed			X			n/a	1.58 (1.32, 1.90)
	# FDs per 1,000 TB, NHW and NHB, birth order-1, 12+ yrs ed			X			n/a	2.69 (2.42, 2.99)
	# FDs per 1,000 TB, NHW and NHB, birth order-2, 12+ yrs ed			X			n/a	2.16 (1.96, 2.39)
	# FDs per 1,000 TB, NHW and NHB, birth order-3, 12+ yrs ed			X			n/a	2.00 (1.81, 2.21)
	# FDs per 1,000 TB, NHW and NHB, birth order-4, 12+ yrs ed			X			n/a	2.13 (1.88, 2.40)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+, 12+ yrs ed			X			n/a	1.84 (1.67, 2.04)
	# FDs per 1,000 TB, NHW and NHB, birth order-1, 12 yrs ed			X			n/a	2.70 (2.31, 3.17)
	# FDs per 1,000 TB, NHW and NHB, birth order-2, 12 yrs ed			X			n/a	2.25 (1.96, 2.58)
	# FDs per 1,000 TB, NHW and NHB, birth order-3, 12 yrs ed			X			n/a	2.22 (1.94, 2.54)
	# FDs per 1,000 TB, NHW and NHB, birth order-4, 12 yrs ed			X			n/a	2.06 (1.75, 2.42)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+, 12 yrs ed			X			n/a	1.73 (1.52, 1.97)
	# FDs per 1,000 TB, NHW and NHB, birth order-1, 13-15 yrs ed			X			n/a	2.32 (1.91, 2.83)
	# FDs per 1,000 TB, NHW and NHB, birth order-2, 13-15 yrs ed			X			n/a	2.07 (1.72, 2.49)
	# FDs per 1,000 TB, NHW and NHB, birth order-3, 13-15 yrs ed			X			n/a	1.62 (1.34, 1.96)
	# FDs per 1,000 TB, NHW and NHB, birth order-4, 13-15 yrs ed			X			n/a	1.89 (1.51, 2.37)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+, 13-15 yrs ed			X			n/a	1.87 (1.55, 2.26)
	# FDs per 1,000 TB, NHW and NHB, birth order-1, 16+ yrs ed			X			n/a	2.76 (2.24, 3.39)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, birth order-21, 16+ yrs ed			X			n/a	1.98 (1.57, 2.49)
	# FDs per 1,000 TB, NHW and NHB, birth order-31, 16+ yrs ed			X			n/a	1.84 (1.39, 2.45)
	# FDs per 1,000 TB, NHW and NHB, birth order-41, 16+ yrs ed			X			n/a	2.88 (2.11, 3.94)
	# FDs per 1,000 TB, NHW and NHB, birth order-5+1, 16+ yrs ed			X			n/a	2.32 (1.70, 3.17)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, no PNC			X	X		n/a	1.66 (1.41, 1.95)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, no PNC			X	X		n/a	1.89 (1.70, 2.09)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, no PNC			X	X		n/a	1.23 (0.92, 1.63)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, any PNC			X	X		n/a	1.48 (1.38, 1.60)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, any PNC			X	X		n/a	1.96 (1.89, 2.04)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, any PNC			X	X		n/a	2.11 (1.91, 2.32)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 1			X	X		n/a	1.60 (1.46, 1.76)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 1			X	X		n/a	2.09 (2.00, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 1			X	X		n/a	2.15 (1.92, 2.41)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 2			X	X		n/a	1.35 (1.19, 1.54)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 2			X	X		n/a	1.59 (1.47, 1.72)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 2			X	X		n/a	1.79 (1.45, 2.23)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 3			X	X		n/a	1.57 (1.13, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 3			X	X		n/a	1.75 (1.45, 2.11)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 3			X	X		n/a	1.86 (1.16, 3.00)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 20-27 wk		X	X			n/a	1.94 (1.76, 2.13)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 20-27 wk		X	X			n/a	2.73 (2.59, 2.87)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 20-27 wk		X	X			n/a	2.40 (2.08, 2.77)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, no PNC, 20-27 wk		X	X	X		n/a	1.99 (1.62, 2.44)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, no PNC, 20-27 wk		X	X	X		n/a	2.32 (2.02, 2.66)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, no PNC, 20-27 wk		X	X	X		n/a	1.45 (0.95, 2.22)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, any PNC, 20-27 wk		X	X	X		n/a	1.73 (1.55, 1.93)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, any PNC, 20-27 wk		X	X	X		n/a	2.50 (2.36, 2.64)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, any PNC, 20-27 wk		X	X	X		n/a	2.30 (1.98, 2.68)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 1, 20-27 wk		X	X	X		n/a	1.91 (1.68, 2.17)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.76 (2.60, 2.94)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.37 (2.01, 2.80)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 2, 20-27 wk		X	X	X		n/a	1.60 (1.29, 1.98)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 2, 20-27 wk		X	X	X		n/a	1.90 (1.67, 2.17)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 2, 20-27 wk		X	X	X		n/a	2.25 (1.53, 3.31)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, 28+ wk		X	X			n/a	1.37 (1.25, 1.50)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, 28+ wk		X	X			n/a	1.83 (1.75, 1.92)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, 28+ wk		X	X			n/a	2.09 (1.85, 2.36)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, no PNC, 28+ wk		X	X	X		n/a	1.29 (0.98, 1.70)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, no PNC, 28+ wk		X	X	X		n/a	1.56 (1.34, 1.82)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, no PNC, 28+ wk		X	X	X		n/a	1.12 (0.75, 1.67)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, any PNC, 28+ wk		X	X	X		n/a	1.35 (1.23, 1.49)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, any PNC, 28+ wk		X	X	X		n/a	1.71 (1.63, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, any PNC, 28+ wk		X	X	X		n/a	2.00 (1.76, 2.27)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 1, 28+ wk		X	X	X		n/a	1.38 (1.21, 1.57)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 1, 28+ wk		X	X	X		n/a	1.73 (1.63, 1.83)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 1, 28+ wk		X	X	X		n/a	2.02 (1.73, 2.36)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 2, 28+ wk		X	X	X		n/a	1.26 (1.08, 1.48)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 2, 28+ wk		X	X	X		n/a	1.47 (1.33, 1.61)
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 2, 28+ wk		X	X	X		n/a	1.63 (1.25, 2.12)
	# FDs per 1,000 TB, NHW and NHB, <20 yrs, PNC start tri 3, 28+ wk		X	X	X		n/a	1.53 (1.09, 2.16)
	# FDs per 1,000 TB, NHW and NHB, 20-34 yrs, PNC start tri 3, 28+ wk		X	X	X		n/a	1.73 (1.42, 2.10)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 35-49 yrs, PNC start tri 3, 28+ wk		X	X	X		n/a	1.72 (1.04, 2.85)
	# FDs per 1,000 TB, NHW and NHB, married, no PNC			X	X		n/a	1.55 (1.26, 1.90)
	# FDs per 1,000 TB, NHW and NHB, unmarried, no PNC			X	X		n/a	1.57 (1.42, 1.72)
	# FDs per 1,000 TB, NHW and NHB, married, any PNC			X	X		n/a	1.73 (1.65, 1.82)
	# FDs per 1,000 TB, NHW and NHB, unmarried, any PNC			X	X		n/a	1.58 (1.51, 1.65)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 1			X	X		n/a	1.85 (1.75, 1.96)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 1			X	X		n/a	1.73 (1.63, 1.83)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 2			X	X		n/a	1.40 (1.24, 1.59)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 2			X	X		n/a	1.36 (1.25, 1.47)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 3			X	X		n/a	1.53 (1.12, 2.10)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 3			X	X		n/a	1.58 (1.31, 1.91)
	# FDs per 1,000 TB, NHW and NHB, married, 20-27 wk			X	X		n/a	2.23 (2.07, 2.40)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 20-27 wk			X	X		n/a	2.03 (1.91, 2.16)
	# FDs per 1,000 TB, NHW and NHB, married, no PNC, 20-27 wk		X	X	X		n/a	1.96 (1.49, 2.56)
	# FDs per 1,000 TB, NHW and NHB, unmarried, no PNC, 20-27 wk		X	X	X		n/a	1.92 (1.68, 2.18)
	# FDs per 1,000 TB, NHW and NHB, married, any PNC, 20-27 wk		X	X	X		n/a	2.24 (2.07, 2.41)
	# FDs per 1,000 TB, NHW and NHB, unmarried, any PNC, 20-27 wk		X	X	X		n/a	1.82 (1.70, 1.95)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.41 (2.22, 2.61)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.00 (1.84, 2.17)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 2, 20-27 wk		X	X	X		n/a	1.88 (1.53, 2.32)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 2, 20-27 wk		X	X	X		n/a	1.41 (1.23, 1.61)
	# FDs per 1,000 TB, NHW and NHB, married, 28+ wk		X	X			n/a	1.46 (1.36, 1.56)
	# FDs per 1,000 TB, NHW and NHB, unmarried, 28+ wk		X	X			n/a	1.55 (1.47, 1.64)
	# FDs per 1,000 TB, NHW and NHB, married, no PNC, 28+ wk		X	X	X		n/a	1.27 (0.92, 1.74)
	# FDs per 1,000 TB, NHW and NHB, unmarried, no PNC, 28+ wk		X	X	X		n/a	1.29 (1.11, 1.49)
	# FDs per 1,000 TB, NHW and NHB, married, any PNC, 28+ wk		X	X	X		n/a	1.46 (1.36, 1.56)
	# FDs per 1,000 TB, NHW and NHB, unmarried, any PNC, 28+ wk		X	X	X		n/a	1.44 (1.36, 1.53)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 1, 28+ wk		X	X	X		n/a	1.50 (1.38, 1.63)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 1, 28+ wk		X	X	X		n/a	1.52 (1.41, 1.65)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 2, 28+ wk		X	X	X		n/a	1.21 (1.03, 1.42)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 2, 28+ wk		X	X	X		n/a	1.32 (1.19, 1.46)
	# FDs per 1,000 TB, NHW and NHB, married, PNC start tri 3, 28+ wk		X	X	X		n/a	1.52 (1.09, 2.13)
	# FDs per 1,000 TB, NHW and NHB, unmarried, PNC start tri 3, 28+ wk		X	X	X		n/a	1.50 (1.23, 1.83)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 1, no PNC			X	X		n/a	2.02 (1.74, 2.35)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 2, no PNC			X	X		n/a	2.17 (1.82, 2.59)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 3, no PNC			X	X		n/a	1.87 (1.53, 2.29)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 4, no PNC			X	X		n/a	1.61 (1.25, 2.07)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 5+, no PNC			X	X		n/a	1.65 (1.38, 1.98)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 1, any PNC			X	X		n/a	1.95 (1.84, 2.06)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 2, any PNC			X	X		n/a	1.96 (1.84, 2.09)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 3, any PNC			X	X		n/a	1.95 (1.81, 2.09)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 4, any PNC			X	X		n/a	1.92 (1.76, 2.11)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 5+, any PNC			X	X		n/a	1.66 (1.53, 1.80)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 1, PNC start tri 1			X	X		n/a	2.12 (1.98, 2.26)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 2, PNC start tri 1			X	X		n/a	2.13 (1.98, 2.30)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 3, PNC start tri 1			X	X		n/a	2.08 (1.92, 2.27)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 4, PNC start tri 1			X	X		n/a	2.15 (1.93, 2.40)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 5+, PNC start tri 1			X	X		n/a	1.76 (1.59, 1.94)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 1, PNC start tri 2			X	X		n/a	1.53 (1.37, 1.71)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 2, PNC start tri 2			X	X		n/a	1.63 (1.43, 1.86)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 3, PNC start tri 2			X	X		n/a	1.67 (1.43, 1.95)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, total-birth order 4, PNC start tri 2			X	X		n/a	1.62 (1.35, 1.94)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 5+, PNC start tri 2			X	X		n/a	1.55 (1.32, 1.81)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 1, PNC start tri 3			X	X		n/a	1.68 (1.26, 2.24)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 2, PNC start tri 3			X	X		n/a	1.56 (1.11, 2.19)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 3, PNC start tri 3			X	X		n/a	2.13 (1.48, 3.06)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 4, PNC start tri 3			X	X		n/a	1.23 (0.79, 1.92)
	# FDs per 1,000 TB, NHW and NHB, total-birth order 5+, PNC start tri 3			X	X		n/a	1.76 (1.26, 2.46)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, no PNC			X	X		n/a	1.72 (1.39, 2.13)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, no PNC			X	X		n/a	1.87 (1.55, 2.25)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, no PNC			X	X		n/a	1.43 (1.07, 1.91)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, any PNC			X	X		n/a	1.72 (1.53, 1.93)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, any PNC			X	X		n/a	2.00 (1.87, 2.14)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, any PNC			X	X		n/a	2.04 (1.90, 2.19)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 1			X	X		n/a	1.67 (1.39, 2.02)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 1			X	X		n/a	1.91 (1.74, 2.11)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 1			X	X		n/a	1.98 (1.80, 2.17)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 2			X	X		n/a	1.60 (1.37, 1.87)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 2			X	X		n/a	1.33 (1.20, 1.47)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 2			X	X		n/a	1.13 (1.00, 1.29)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 3			X	X		n/a	2.04 (1.40, 2.99)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 3			X	X		n/a	1.59 (1.08, 2.34)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 3			X	X		n/a	1.33 (0.83, 2.13)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, 20-27 wk		X	X			n/a	2.57 (2.17, 3.03)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, 20-27 wk		X	X			n/a	2.62 (2.37, 2.88)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, 20-27 wk		X	X			n/a	2.90 (2.62, 3.21)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, no PNC, 20-27 wk		X	X	X		n/a	1.97 (1.45, 2.69)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, no PNC, 20-27 wk		X	X	X		n/a	2.24 (1.71, 2.92)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, no PNC, 20-27 wk		X	X	X		n/a	2.59 (1.76, 3.80)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, any PNC, 20-27 wk		X	X	X		n/a	2.19 (1.80, 2.66)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, any PNC, 20-27 wk		X	X	X		n/a	2.24 (2.01, 2.49)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, any PNC, 20-27 wk		X	X	X		n/a	2.50 (2.24, 2.79)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.19 (1.64, 2.92)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.37 (2.06, 2.73)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 1, 20-27 wk		X	X	X		n/a	2.47 (2.17, 2.81)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 2, 20-27 wk		X	X	X		n/a	2.00 (1.53, 2.62)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 2, 20-27 wk		X	X	X		n/a	1.43 (1.21, 1.69)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 2, 20-27 wk		X	X	X		n/a	1.41 (1.15, 1.72)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, 28+ wk		X	X			n/a	1.66 (1.46, 1.89)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, 28+ wk		X	X			n/a	2.02 (1.86, 2.20)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, 28+ wk		X	X			n/a	1.81 (1.64, 2.00)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, no PNC, 28+ wk		X	X	X		n/a	1.65 (1.22, 2.22)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, no PNC, 28+ wk		X	X	X		n/a	1.72 (1.32, 2.24)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, any PNC, 28+ wk		X	X	X		n/a	1.56 (1.35, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, any PNC, 28+ wk		X	X	X		n/a	1.88 (1.71, 2.05)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, any PNC, 28+ wk		X	X	X		n/a	1.77 (1.60, 1.96)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 1, 28+ wk		X	X	X		n/a	1.39 (1.08, 1.78)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 1, 28+ wk		X	X	X		n/a	1.64 (1.43, 1.88)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 1, 28+ wk		X	X	X		n/a	1.58 (1.39, 1.81)
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 2, 28+ wk		X	X	X		n/a	1.47 (1.21, 1.78)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 2, 28+ wk		X	X	X		n/a	1.29 (1.13, 1.47)
	# FDs per 1,000 TB, NHW and NHB, 13+ yrs ed, PNC start tri 2, 28+ wk		X	X	X		n/a	1.01 (0.86, 1.19)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, <12 yrs ed, PNC start tri 3, 28+ wk		X	X	X		n/a	1.92 (1.29, 2.87)
	# FDs per 1,000 TB, NHW and NHB, 12 yrs ed, PNC start tri 3, 28+ wk		X	X	X		n/a	1.62 (1.07, 2.44)
Hsieh 1997	# FDs per 1000 TB, W and B, 1989-1990		X				n/a	2.07
	# FDs per 1000 TB, W and B, 1979-1980		X				n/a	1.78
	# FDs per 1000 TB, W and B, 1981-1982		X				n/a	1.75
	# FDs per 1000 TB, W and B, 1983-1984		X				n/a	1.78
	# FDs per 1000 TB, W and B, 1985-1986		X				n/a	1.83
	# FDs per 1000 TB, W and B, 1987-1988		X				n/a	1.96
	# FDs per 1000 TB, W and B, 1989-1990, <1500g		X				n/a	0.84
	# FDs per 1000 TB, W and B, 1979-1980, <1500g		X				n/a	0.9
	# FDs per 1000 TB, W and B, 1989-1990, 1500-2499g		X				n/a	0.94
	# FDs per 1000 TB, W and B, 1979-1980, 1500-2499g		X				n/a	0.88
	# FDs per 1000 TB, W and B, 1989-1990, 2500-3999g		X				n/a	1.24
	# FDs per 1000 TB, W and B, 1979-1980, 2500-3999g		X				n/a	1.21
	# FDs per 1000 TB, W and B, 1989-1990, 4000+g		X				n/a	2.75
	# FDs per 1000 TB, W and B, 1979-1980, 4000+g		X				n/a	2.96
	# FDs per 1000 TB, W and B, 1989-1990 BW not stated		X				n/a	1.20
	# FDs per 1000 TB, W and B, 1979-1980 BW not stated		X				n/a	1.31
Kallan 2001	# FDs per 1000 TB, NHW and NHB, native-born			X			n/a	2.40 (2.23, 2.57)
	# FDs per 1000 TB, NHW and NHB, non-native-born			X			n/a	1.61 (1.35, 1.97)
Koonin 1997	% preg-related mat deaths with SB, W and B						n/a	.67 (0.18, 2.52)
Kramer 2002	# FDs per 1000 LB plus FDs, W and B						n/a	1.83 (1.79, 1.86)
Larkin 2018	# IUFDs per 1000, NHW and NHB						n/a	2.15 (2.12, 2.20)
Lemon 2016	# SB per 1,000 LB and SB, NHW and NHB						n/a	2.31 (2.15, 2.50)
Lorch 2012	OR for FD (NHB v NHW)	X					unadjusted	2.24 (2.08, 2.42)
	OR for FD (chorioamnionitis v none)	X		X			age, insurance, PNC, ed, preexisting cond	0.96
	OR for FD (preg induced hypert v none)	X		X			age, insurance, PNC, ed, preexisting cond, chorioamnionitis, cord abnormalities, cord prolapse, disorders of placentation, eclampsia, oligohydramnios, placenta abruption, placenta previa	1.32
MacDorman and Hoyert 2007	# FDs per 1,000 TB, NHW and NHB, 20-27 wk		X				n/a	2.77 (2.66, 2.88)
	# FDs per 1,000 TB, NHW and NHB, 28+ wk		X				n/a	1.94 (1.86, 2.03)
	# FDs per 1,000 TB, NHW and NHB, singleton		X				n/a	2.43 (2.36, 2.51)
	# FDs per 1,000 TB, NHW and NHB, twin		X				n/a	1.64 (1.47, 1.82)
	# FDs per 1,000 TB, NHW and NHB, triplet or higher order		X				n/a	1.75 (1.10, 2.76)
	# FDs per 1,000 TB, NHW and NHB, male		X				n/a	2.41 (2.31, 2.51)
	# FDs per 1,000 TB, NHW and NHB, female		X				n/a	2.27 (2.17, 2.37)
	# FDs per 1,000 TB, NHW and NHB, married			X			n/a	2.36 (2.23, 2.51)
	# FDs per 1,000 TB, NHW and NHB, unmarried			X			n/a	1.82 (1.74, 1.92)
	# FDs per 1,000 TB, NHW and NHB, less than 15 yrs			X			n/a	0.86 (0.51, 1.44)
	# FDs per 1,000 TB, NHW and NHB, 15–19 yrs			X			n/a	1.77 (1.62, 1.93)
	# FDs per 1,000 TB, NHW and NHB, 15–17 yrs			X			n/a	1.55 (1.34, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 18–19 yrs			X			n/a	1.86 (1.67, 2.07)
	# FDs per 1,000 TB, NHW and NHB, 20–24 yrs			X			n/a	2.03 (1.91, 2.15)
	# FDs per 1,000 TB, NHW and NHB, 25–29 yrs			X			n/a	2.64 (2.48, 2.82)
	# FDs per 1,000 TB, NHW and NHB, 30–34 yrs			X			n/a	2.67 (2.49, 2.85)
	# FDs per 1,000 TB, NHW and NHB, 35–39 yrs			X			n/a	2.90 (2.66, 3.15)
	# FDs per 1,000 TB, NHW and NHB, 40–44 yrs			X			n/a	2.36 (2.03, 2.75)
	# FDs per 1,000 TB, NHW and NHB, 45 yrs and over			X			n/a	3.17 (1.89, 5.33)
	# FDs per 1,000 TB, NHW and NHB, 15–19 yrs, 20-27 wk		X	X			n/a	1.96 (1.75, 2.21)
	# FDs per 1,000 TB, NHW and NHB, 15–17 yrs, 20-27 wk		X	X			n/a	1.85 (1.52, 2.26)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 18–19 yrs, 20-27 wk		X	X			n/a	1.99 (1.72, 2.30)
	# FDs per 1,000 TB, NHW and NHB, 20–24 yrs, 20-27 wk		X	X			n/a	2.44 (2.24, 2.65)
	# FDs per 1,000 TB, NHW and NHB, 25–29 yrs, 20-27 wk		X	X			n/a	3.06 (2.81, 3.33)
	# FDs per 1,000 TB, NHW and NHB, 30–34 yrs, 20-27 wk		X	X			n/a	3.23 (2.94, 3.53)
	# FDs per 1,000 TB, NHW and NHB, 35–39 yrs, 20-27 wk		X	X			n/a	3.59 (3.21, 4.03)
	# FDs per 1,000 TB, NHW and NHB, 40–44 yrs, 20-27 wk		X	X			n/a	2.86 (2.33, 3.50)
	# FDs per 1,000 TB, NHW and NHB, 15–19 yrs, 28+ wk		X	X			n/a	1.57 (1.38, 1.78)
	# FDs per 1,000 TB, NHW and NHB, 15–17 yrs, 28+ wk		X	X			n/a	1.25 (1.00, 1.56)
	# FDs per 1,000 TB, NHW and NHB, 18–19 yrs, 28+ wk		X	X			n/a	1.74 (1.49, 2.03)
	# FDs per 1,000 TB, NHW and NHB, 20–24 yrs, 28+ wk		X	X			n/a	1.68 (1.54, 1.83)
	# FDs per 1,000 TB, NHW and NHB, 25–29 yrs, 28+ wk		X	X			n/a	2.26 (2.06, 2.48)
	# FDs per 1,000 TB, NHW and NHB, 30–34 yrs, 28+ wk		X	X			n/a	2.12 (1.91, 2.36)
	# FDs per 1,000 TB, NHW and NHB, 35–39 yrs, 28+ wk		X	X			n/a	2.28 (2.00, 2.59)
	# FDs per 1,000 TB, NHW and NHB, 40–44 yrs, 28+ wk		X	X			n/a	1.90 (1.50, 2.40)
	# FDs per 1,000 TB, NHW and NHB, less than 500 g		X				n/a	0.88 (0.85, 0.92)
	# FDs per 1,000 TB, NHW and NHB, 500–749 g		X				n/a	0.81 (0.76, 0.87)
	# FDs per 1,000 TB, NHW and NHB, 750–999 g		X				n/a	0.87 (0.78, 0.98)
	# FDs per 1,000 TB, NHW and NHB, 1,000–1,249 g		X				n/a	1.03 (0.90, 1.18)
	# FDs per 1,000 TB, NHW and NHB, 1,250–1,499 g		X				n/a	1.15 (0.99, 1.34)
	# FDs per 1,000 TB, NHW and NHB, 1,500–1,999 g		X				n/a	1.28 (1.15, 1.43)
	# FDs per 1,000 TB, NHW and NHB, 2,000–2,499 g		X				n/a	1.30 (1.16, 1.45)
	# FDs per 1,000 TB, NHW and NHB, 2,500–2,999 g		X				n/a	1.03 (0.91, 1.17)
	# FDs per 1,000 TB, NHW and NHB, 3,000–3,499 g		X				n/a	1.28 (1.10, 1.49)
	# FDs per 1,000 TB, NHW and NHB, 3,500–3,999 g		X				n/a	1.98 (1.62, 2.43)
	# FDs per 1,000 TB, NHW and NHB, 4,000 g or more		X				n/a	3.65 (2.81, 4.73)
MacDorman and Kirmeyer 2009b	# FDs per 1,000 TB, NHW and NHB, singleton		X				n/a	2.41 (2.34, 2.49)
	# FDs per 1,000 TB, NHW and NHB, twin		X				n/a	1.66 (1.49, 1.84)
	# FDs per 1,000 TB, NHW and NHB, triplet or higher order		X				n/a	2.17 (1.45, 3.25)
	# FDs per 1,000 TB, NHW and NHB, male		X				n/a	2.39 (2.29, 2.49)
	# FDs per 1,000 TB, NHW and NHB, female		X				n/a	2.26 (2.16, 2.36)
	# FDs per 1,000 TB, NHW and NHB, married			X			n/a	2.47 (2.33, 2.63)
	# FDs per 1,000 TB, NHW and NHB, unmarried			X			n/a	1.72 (1.63, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs			X			n/a	1.74 (1.60, 1.89)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs			X			n/a	1.55 (1.34, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs			X			n/a	1.81 (1.63, 2.01)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs			X			n/a	2.09 (1.97, 2.22)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs			X			n/a	2.31 (2.17, 2.46)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs			X			n/a	3.02 (2.82, 3.23)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs			X			n/a	2.81 (2.58, 3.06)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs			X			n/a	2.33 (2.01, 2.71)
	# FDs per 1,000 TB, NHW and NHB, 20-27 wk		X				n/a	2.71 (2.60, 2.83)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 20-27 wk		X	X			n/a	1.99 (1.78, 2.24)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 20-27 wk		X	X			n/a	1.74 (1.42, 2.13)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 20-27 wk		X	X			n/a	2.10 (1.83, 2.42)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 20-27 wk		X	X			n/a	2.45 (2.25, 2.67)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 20-27 wk		X	X			n/a	2.69 (2.47, 2.93)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 20-27 wk		X	X			n/a	3.54 (3.23, 3.88)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 20-27 wk		X	X			n/a	3.32 (2.95, 3.72)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 20-27 wk		X	X			n/a	2.74 (2.22, 3.36)
	# FDs per 1,000 TB, NHW and NHB, 28+ wk		X				n/a	1.96 (1.87, 2.05)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 28+ wk		X	X			n/a	1.47 (1.30, 1.67)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 28+ wk		X	X			n/a	1.35 (1.08, 1.69)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 28+ wk		X	X			n/a	1.52 (1.30, 1.78)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 28+ wk		X	X			n/a	1.79 (1.64, 1.95)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 28+ wk		X	X			n/a	1.95 (1.77, 2.14)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 28+ wk		X	X			n/a	2.51 (2.26, 2.78)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 28+ wk		X	X			n/a	2.34 (2.06, 2.66)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 28+ wk		X	X			n/a	2.00 (1.60, 2.48)
	# FDs per 1,000 TB, NHW and NHB, <500 g		X				n/a	0.88 (0.84, 0.91)
	# FDs per 1,000 TB, NHW and NHB, 500-749g		X				n/a	0.79 (0.74, 0.85)
	# FDs per 1,000 TB, NHW and NHB, 750-999g		X				n/a	0.86 (0.77, 0.97)
	# FDs per 1,000 TB, NHW and NHB, 1000-1249g		X				n/a	1.03 (0.89, 1.18)
	# FDs per 1,000 TB, NHW and NHB, 1250-1499g		X				n/a	1.22 (1.05, 1.42)
	# FDs per 1,000 TB, NHW and NHB, 1500-1999g		X				n/a	1.25 (1.11, 1.39)
	# FDs per 1,000 TB, NHW and NHB, 2000-2499g		X				n/a	1.10 (0.97, 1.24)
	# FDs per 1,000 TB, NHW and NHB, 2500-2999g		X				n/a	1.06 (0.94, 1.21)
	# FDs per 1,000 TB, NHW and NHB, 3000-3499g		X				n/a	1.23 (1.05, 1.44)
	# FDs per 1,000 TB, NHW and NHB, 3500-3999g		X				n/a	2.09 (1.67, 2.62)
	# FDs per 1,000 TB, NHW and NHB, 4000+g		X				n/a	4.25 (3.26, 5.53)
	# FDs per 1,000 TB, NHW and NHB, 20-23 wk		X				n/a	0.85 (0.82, 0.88)
	# FDs per 1,000 TB, NHW and NHB, 24-27 wk		X				n/a	0.81 (0.75, 0.87)
	# FDs per 1,000 TB, NHW and NHB, 28-31 wk		X				n/a	1.15 (1.05, 1.25)
	# FDs per 1,000 TB, NHW and NHB, 32-33 wk		X				n/a	1.34 (1.19, 1.51)
	# FDs per 1,000 TB, NHW and NHB, 34-36 wk		X				n/a	1.28 (1.16, 1.41)
	# FDs per 1,000 TB, NHW and NHB, 37-39 wk		X				n/a	1.81 (1.65, 1.98)
	# FDs per 1,000 TB, NHW and NHB, 40 wk		X				n/a	1.59 (1.28, 1.98)
	# FDs per 1,000 TB, NHW and NHB, 41 wk		X				n/a	1.65 (1.22, 2.24)
	# FDs per 1,000 TB, NHW and NHB, 42+ wk		X				n/a	1.57 (1.19, 2.06)
MacDorman and Munson 2007	# FDs per 1,000 TB, NHW and NHB, singleton		X				n/a	2.33 (2.25, 2.40)
	# FDs per 1,000 TB, NHW and NHB, twin		X				n/a	1.73 (1.55, 1.93)
	# FDs per 1,000 TB, NHW and NHB, triplet or higher order		X				n/a	2.64 (1.88, 3.72)
	# FDs per 1,000 TB, NHW and NHB, male		X				n/a	2.29 (2.20, 2.39)
	# FDs per 1,000 TB, NHW and NHB, female		X				n/a	2.23 (2.13, 2.33)
	# FDs per 1,000 TB, NHW and NHB, married			X			n/a	2.30 (2.17, 2.44)
	# FDs per 1,000 TB, NHW and NHB, unmarried			X			n/a	1.78 (1.69, 1.87)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs			X			n/a	1.71 (1.57, 1.86)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs			X			n/a	1.56 (1.35, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs			X			n/a	1.76 (1.58, 1.95)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs			X			n/a	2.07 (1.95, 2.19)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs			X			n/a	2.34 (2.20, 2.49)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs			X			n/a	2.80 (2.61, 2.99)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs			X			n/a	2.59 (2.38, 2.83)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs			X			n/a	2.14 (1.83, 2.51)
	# FDs per 1,000 TB, NHW and NHB, 45+ yrs			X			n/a	3.51 (2.09, 5.88)
	# FDs per 1,000 TB, NHW and NHB, 20-27 wk		X				n/a	2.67 (2.56, 2.79)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 20-27 wk		X	X			n/a	1.84 (1.64, 2.07)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 20-27 wk		X	X			n/a	1.65 (1.36, 2.01)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 20-27 wk		X	X			n/a	1.91 (1.65, 2.21)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 20-27 wk		X	X			n/a	2.44 (2.25, 2.66)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 20-27 wk		X	X			n/a	2.88 (2.64, 3.14)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 20-27 wk		X	X			n/a	3.44 (3.14, 3.77)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 20-27 wk		X	X			n/a	3.13 (2.78, 3.53)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 20-27 wk		X	X			n/a	2.12 (1.68, 2.67)
	# FDs per 1,000 TB, NHW and NHB, 28+ wk		X				n/a	1.90 (1.81, 1.98)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 28+ wk		X	X			n/a	1.58 (1.40, 1.79)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 28+ wk		X	X			n/a	1.47 (1.18, 1.82)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 28+ wk		X	X			n/a	1.62 (1.39, 1.89)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 28+ wk		X	X			n/a	1.76 (1.61, 1.91)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 28+ wk		X	X			n/a	1.88 (1.71, 2.06)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 28+ wk		X	X			n/a	2.18 (1.96, 2.42)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 28+ wk		X	X			n/a	2.12 (1.86, 2.42)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 28+ wk		X	X			n/a	2.19 (1.76, 2.71)
	# FDs per 1,000 TB, NHW and NHB, <500 g		X				n/a	0.87 (0.84, 0.90)
	# FDs per 1,000 TB, NHW and NHB, 500-749g		X				n/a	0.82 (0.76, 0.88)
	# FDs per 1,000 TB, NHW and NHB, 750-999g		X				n/a	0.87 (0.77, 0.98)
	# FDs per 1,000 TB, NHW and NHB, 1000-1249g		X				n/a	1.02 (0.89, 1.17)
	# FDs per 1,000 TB, NHW and NHB, 1250-1499g		X				n/a	1.02 (0.87, 1.21)
	# FDs per 1,000 TB, NHW and NHB, 1500-1999g		X				n/a	1.28 (1.15, 1.43)
	# FDs per 1,000 TB, NHW and NHB, 2000-2499g		X				n/a	1.15 (1.03, 1.29)
	# FDs per 1,000 TB, NHW and NHB, 2500-2999g		X				n/a	1.04 (0.92, 1.18)
	# FDs per 1,000 TB, NHW and NHB, 3000-3499g		X				n/a	1.24 (1.07, 1.43)
	# FDs per 1,000 TB, NHW and NHB, 3500-3999g		X				n/a	2.29 (1.87, 2.80)
	# FDs per 1,000 TB, NHW and NHB, 4000+g		X				n/a	3.89 (3.04, 4.97)
	# FDs per 1,000 TB, NHW and NHB, 20-23 wk		X				n/a	0.86 (0.83, 0.89)
	# FDs per 1,000 TB, NHW and NHB, 24-27 wk		X				n/a	0.82 (0.76, 0.88)
	# FDs per 1,000 TB, NHW and NHB, 28-31 wk		X				n/a	1.12 (1.03, 1.22)
	# FDs per 1,000 TB, NHW and NHB, 32-35 wk		X				n/a	1.40 (1.29, 1.52)
	# FDs per 1,000 TB, NHW and NHB, 36 wk		X				n/a	1.22 (1.04, 1.43)
	# FDs per 1,000 TB, NHW and NHB, 37-39 wk		X				n/a	1.72 (1.57, 1.88)
	# FDs per 1,000 TB, NHW and NHB, 40 wk		X				n/a	1.50 (1.22, 1.85)
	# FDs per 1,000 TB, NHW and NHB, 41 wk		X				n/a	1.58 (1.19, 2.10)
	# FDs per 1,000 TB, NHW and NHB, 42+ wk		X				n/a	1.54 (1.19, 1.98)
MacDorman 2011	# FDs of 20 wk of gestation or more per 1000 LB and FDs, NHW and NHB						n/a	2.32
MacDorman 2012	# FDs per 1,000 TB, NHW and NHB, 1999		X				n/a	2.27 (2.20, 2.33)
	# FDs per 1,000 TB, NHW and NHB, 1998		X				n/a	2.17 (2.10, 2.23)
	# FDs per 1,000 TB, NHW and NHB, 1997		X				n/a	2.17 (2.10, 2.23)
	# FDs per 1,000 TB, NHW and NHB, 1996		X				n/a	2.07 (2.01, 2.13)
	# FDs per 1,000 TB, NHW and NHB, singleton		X				n/a	2.30 (2.23, 2.38)
	# FDs per 1,000 TB, NHW and NHB, twin		X				n/a	1.69 (1.52, 1.87)
	# FDs per 1,000 TB, NHW and NHB, triplet or higher order		X				n/a	1.75 (1.13, 2.73)
	# FDs per 1,000 TB, NHW and NHB, male		X				n/a	2.34 (2.25, 2.44)
	# FDs per 1,000 TB, NHW and NHB, female		X				n/a	2.12 (2.02, 2.21)
	# FDs per 1,000 TB, NHW and NHB, married			X			n/a	2.45 (2.32, 2.59)
	# FDs per 1,000 TB, NHW and NHB, unmarried			X			n/a	1.66 (1.59, 1.73)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs			X			n/a	1.64 (1.51, 1.79)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs			X			n/a	1.61 (1.39, 1.87)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs			X			n/a	1.64 (1.48, 1.82)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs			X			n/a	1.91 (1.80, 2.02)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs			X			n/a	2.40 (2.26, 2.55)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs			X			n/a	2.84 (2.65, 3.05)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs			X			n/a	2.70 (2.48, 2.95)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs			X			n/a	2.15 (1.83, 2.53)
	# FDs per 1,000 TB, NHW and NHB, 20-27 wk		X				n/a	2.62 (2.52, 2.73)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 20-27 wk		X	X			n/a	1.87 (1.67, 2.10)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 20-27 wk		X	X			n/a	1.77 (1.45, 2.15)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 20-27 wk		X	X			n/a	1.88 (1.62, 2.17)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 20-27 wk		X	X			n/a	2.37 (2.19, 2.58)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 20-27 wk		X	X			n/a	2.77 (2.55, 3.01)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 20-27 wk		X	X			n/a	3.30 (3.00, 3.63)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 20-27 wk		X	X			n/a	3.23 (2.87, 3.63)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 20-27 wk		X	X			n/a	2.23 (1.78, 2.78)
	# FDs per 1,000 TB, NHW and NHB, 28+ wk		X				n/a	1.88 (1.79, 1.96)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 28+ wk		X	X			n/a	1.41 (1.24, 1.60)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 28+ wk		X	X			n/a	1.43 (1.14, 1.80)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 28+ wk		X	X			n/a	1.41 (1.21, 1.65)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 28+ wk		X	X			n/a	1.52 (1.39, 1.65)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 28+ wk		X	X			n/a	2.06 (1.89, 2.25)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 28+ wk		X	X			n/a	2.41 (2.17, 2.68)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 28+ wk		X	X			n/a	2.21 (1.93, 2.52)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 28+ wk		X	X			n/a	2.10 (1.66, 2.65)
	# FDs per 1,000 TB, NHW and NHB, <500 g		X				n/a	0.85 (0.82, 0.88)
	# FDs per 1,000 TB, NHW and NHB, 500-749g		X				n/a	0.82 (0.77, 0.88)
	# FDs per 1,000 TB, NHW and NHB, 750-999g		X				n/a	0.80 (0.71, 0.90)
	# FDs per 1,000 TB, NHW and NHB, 1000-1249g		X				n/a	1.08 (0.94, 1.24)
	# FDs per 1,000 TB, NHW and NHB, 1250-1499g		X				n/a	1.23 (1.06, 1.43)
	# FDs per 1,000 TB, NHW and NHB, 1500-1999g		X				n/a	1.10 (0.99, 1.22)
	# FDs per 1,000 TB, NHW and NHB, 2000-2499g		X				n/a	1.06 (0.94, 1.19)
	# FDs per 1,000 TB, NHW and NHB, 2500-2999g		X				n/a	1.11 (0.98, 1.26)
	# FDs per 1,000 TB, NHW and NHB, 3000-3499g		X				n/a	1.25 (1.08, 1.45)
	# FDs per 1,000 TB, NHW and NHB, 3500-3999g		X				n/a	1.76 (1.42, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 4000+g		X				n/a	4.18 (3.25, 5.36)
	# FDs per 1,000 TB, NHW and NHB, 20-23 wk		X				n/a	0.85 (0.73, 0.99)
	# FDs per 1,000 TB, NHW and NHB, 24-27 wk		X				n/a	0.78 (0.64, 0.94)
	# FDs per 1,000 TB, NHW and NHB, 28-31 wk		X				n/a	1.13 (0.92, 1.38)
	# FDs per 1,000 TB, NHW and NHB, 32-33 wk		X				n/a	1.19 (0.97, 1.47)
	# FDs per 1,000 TB, NHW and NHB, 34-36 wk		X				n/a	1.31 (1.06, 1.60)
	# FDs per 1,000 TB, NHW and NHB, 37-39 wk		X				n/a	1.62 (1.32, 1.98)
	# FDs per 1,000 TB, NHW and NHB, 40 wk		X				n/a	1.84 (1.47, 2.30)
	# FDs per 1,000 TB, NHW and NHB, 41 wk		X				n/a	1.91 (1.48, 2.46)
	# FDs per 1,000 TB, NHW and NHB, 42+ wk		X				n/a	1.45 (1.15, 1.84)
MacDorman 2015	# FDs per 1,000 TB, NHW and NHB, 2013		X				n/a	2.16 (2.09, 2.23)
	# FDs per 1,000 TB, NHW and NHB, 2012		X				n/a	2.17 (2.11, 2.24)
	# FDs per 1,000 TB, NHW and NHB, 2011		X				n/a	2.18 (2.12, 2.25)
	# FDs per 1,000 TB, NHW and NHB, 2010		X				n/a	2.25 (2.18, 2.32)
	# FDs per 1,000 TB, NHW and NHB, 2009		X				n/a	2.17 (2.11, 2.24)
	# FDs per 1,000 TB, NHW and NHB, 2008		X				n/a	2.27 (2.20, 2.34)
	# FDs per 1,000 TB, NHW and NHB, 2007		X				n/a	2.29 (2.23, 2.36)
	# FDs per 1,000 TB, NHW and NHB, 2006		X				n/a	2.23 (2.16, 2.30)
	# FDs per 1,000 TB, NHW and NHB, 2005		X				n/a	2.32 (2.25, 2.40)
	# FDs per 1,000 TB, NHW and NHB, 2004		X				n/a	2.27 (2.20, 2.34)
	# FDs per 1,000 TB, NHW and NHB, 2003		X				n/a	2.35 (2.28, 2.42)
	# FDs per 1,000 TB, NHW and NHB, 2002		X				n/a	2.23 (2.17, 2.30)
	# FDs per 1,000 TB, NHW and NHB, 2001		X				n/a	2.24 (2.17, 2.30)
	# FDs per 1,000 TB, NHW and NHB, 2000		X				n/a	2.28 (2.21, 2.34)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 1995		X				n/a	2.15 (2.09, 2.21)
	# FDs per 1,000 TB, NHW and NHB, married			X			n/a	2.18 (2.05, 2.31)
	# FDs per 1,000 TB, NHW and NHB, unmarried			X			n/a	1.72 (1.65, 1.80)
	# FDs per 1,000 TB, NHW and NHB, singleton		X				n/a	2.19 (2.12, 2.27)
	# FDs per 1,000 TB, NHW and NHB, twin		X				n/a	1.81 (1.62, 2.02)
	# FDs per 1,000 TB, NHW and NHB, triplet or higher order		X				n/a	2.19 (1.48, 3.24)
	# FDs per 1,000 TB, NHW and NHB, male		X				n/a	2.24 (2.15, 2.34)
	# FDs per 1,000 TB, NHW and NHB, female		X				n/a	2.07 (1.98, 2.17)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs			X			n/a	1.83 (1.64, 2.05)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs			X			n/a	1.76 (1.42, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs			X			n/a	1.85 (1.63, 2.11)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs			X			n/a	1.90 (1.78, 2.02)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs			X			n/a	2.21 (2.08, 2.35)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs			X			n/a	2.47 (2.32, 2.64)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs			X			n/a	2.38 (2.17, 2.59)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs			X			n/a	2.31 (1.99, 2.68)
	# FDs per 1,000 TB, NHW and NHB, 45+ yrs			X			n/a	2.34 (1.47, 3.72)
	# FDs per 1,000 TB, NHW and NHB, 20-27 wk		X				n/a	2.56 (2.45, 2.68)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 20-27 wk		X	X			n/a	1.92 (1.64, 2.23)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 20-27 wk		X	X			n/a	1.92 (1.45, 2.55)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 20-27 wk		X	X			n/a	1.89 (1.57, 2.27)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 20-27 wk		X	X			n/a	2.25 (2.06, 2.46)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 20-27 wk		X	X			n/a	2.64 (2.42, 2.88)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 20-27 wk		X	X			n/a	3.14 (2.87, 3.43)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 20-27 wk		X	X			n/a	2.79 (2.47, 3.15)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 20-27 wk		X	X			n/a	2.55 (2.08, 3.12)
	# FDs per 1,000 TB, NHW and NHB, 28+ wk		X				n/a	1.81 (1.73, 1.89)
	# FDs per 1,000 TB, NHW and NHB, 15-19 yrs, 28+ wk		X	X			n/a	1.75 (1.50, 2.05)
	# FDs per 1,000 TB, NHW and NHB, 15-17 yrs, 28+ wk		X	X			n/a	1.56 (1.12, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 18-19 yrs, 28+ wk		X	X			n/a	1.82 (1.52, 2.18)
	# FDs per 1,000 TB, NHW and NHB, 20-24 yrs, 28+ wk		X	X			n/a	1.60 (1.46, 1.75)
	# FDs per 1,000 TB, NHW and NHB, 25-29 yrs, 28+ wk		X	X			n/a	1.85 (1.69, 2.02)
	# FDs per 1,000 TB, NHW and NHB, 30-34 yrs, 28+ wk		X	X			n/a	1.88 (1.70, 2.08)
	# FDs per 1,000 TB, NHW and NHB, 35-39 yrs, 28+ wk		X	X			n/a	2.01 (1.76, 2.29)
	# FDs per 1,000 TB, NHW and NHB, 40-44 yrs, 28+ wk		X	X			n/a	2.10 (1.69, 2.61)
	# FDs per 1,000 TB, NHW and NHB, <500 g		X				n/a	0.86 (0.83, 0.89)
	# FDs per 1,000 TB, NHW and NHB, 500-749g		X				n/a	0.83 (0.76, 0.89)
	# FDs per 1,000 TB, NHW and NHB, 750-999g		X				n/a	0.82 (0.73, 0.93)
	# FDs per 1,000 TB, NHW and NHB, 1000-1249g		X				n/a	0.89 (0.77, 1.03)
	# FDs per 1,000 TB, NHW and NHB, 1250-1499g		X				n/a	1.12 (0.96, 1.31)
	# FDs per 1,000 TB, NHW and NHB, 1500-1999g		X				n/a	1.20 (1.07, 1.34)
	# FDs per 1,000 TB, NHW and NHB, 2000-2499g		X				n/a	1.02 (0.90, 1.15)
	# FDs per 1,000 TB, NHW and NHB, 2500-2999g		X				n/a	.95 (0.83, 1.07)
	# FDs per 1,000 TB, NHW and NHB, 3000-3499g		X				n/a	1.34 (1.16, 1.55)
	# FDs per 1,000 TB, NHW and NHB, 3500-3999g		X				n/a	2.34 (1.91, 2.87)
	# FDs per 1,000 TB, NHW and NHB, 4000+g		X				n/a	3.68 (2.86, 4.73)
	# FDs per 1,000 TB, NHW and NHB, 20-23 wk		X				n/a	0.85 (0.82, 0.88)
	# FDs per 1,000 TB, NHW and NHB, 24-27 wk		X				n/a	0.88 (0.82, 0.95)
	# FDs per 1,000 TB, NHW and NHB, 28-31 wk		X				n/a	1.13 (1.04, 1.23)
	# FDs per 1,000 TB, NHW and NHB, 32-33 wk		X				n/a	1.21 (1.07, 1.37)
	# FDs per 1,000 TB, NHW and NHB, 34-36 wk		X				n/a	1.30 (1.18, 1.42)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	# FDs per 1,000 TB, NHW and NHB, 37-38 wk		X				n/a	1.35 (1.21, 1.50)
	# FDs per 1,000 TB, NHW and NHB, 39-40 wk		X				n/a	1.53 (1.34, 1.74)
	# FDs per 1,000 TB, NHW and NHB, 41 wk		X				n/a	1.44 (1.04, 2.00)
	# FDs per 1,000 TB, NHW and NHB, 42+ wk		X				n/a	1.95 (1.49, 2.57)
Meyer 1999	# FDs per 1,000 LB and FDs, W and B, 1995-1997		X				n/a	2.34
	# FDs per 1,000 LB and FDs, W and B, 1995-1997, singleton		X				n/a	2.43
	# FDs per 1,000 LB and FDs, W and B, 1995-1997, multiple		X				n/a	1.56
	# FDs per 1,000 LB and FDs, W and B, 1980-1982		X				n/a	1.76
	# FDs per 1,000 LB and FDs, W and B, 1980-1982, singleton		X				n/a	1.78
	# FDs per 1,000 LB and FDs, W and B, 1980-1982, multiple		X				n/a	1.18
Nabukera 2009	OR for FD (AA v W)	X					marital, ed, PNC, BMI, smoking, chronic hyperten, diab, gestational hyperten, past adverse outcome, yr of first birth	2.02 (1.63, 2.51)
Powell-Griner 1989	# late FDs per 1000 LB and specified FDs, W and B, 1985		X				n/a	1.58 (1.53, 1.63)
	# late FDs per 1000 LB and specified FDs, W and B, 1984		X				n/a	1.52 (1.47, 1.57)
	# late FDs per 1000 LB and specified FDs, W and B, 1983		X				n/a	1.54 (1.49, 1.59)
	# late FDs per 1000 LB and specified FDs, W and B, 1982		X				n/a	1.50 (1.45, 1.55)
	# late FDs per 1000 LB and specified FDs, W and B, 1981		X				n/a	1.49 (1.44, 1.54)
	# late FDs per 1000 LB and specified FDs, W and B, 1980		X				n/a	1.56 (1.51, 1.61)
	# late FDs per 1000 LB and specified FDs, W and B, 1979		X				n/a	1.53 (1.48, 1.57)
Pruitt 2020	RaR for FD of unspecified cause (B v W)	X	X				unadjusted	2.00 (1.90, 2.10)
	RaR for FD from mat cond unrelated to preg (B v W)	X	X				unadjusted	3.4 (3.2, 3.6)
	RaR for FD from mat comp of preg (B v W)	X	X				unadjusted	3.1 (2.9, 3.2)
	RaR for FD from syndrome of infant of a diabetic mother and neonatal diab mellitus (B v W)	X	X				unadjusted	2.8 (2.4, 3.2)
	RaR for FD from comp of placenta, cord, and membranes (B v W)	X	X				unadjusted	2.0 (1.9, 2.0)
Rammah 2019	HR for SB (ozone, per IQR increase)	X				X	unadjusted	0.97
Reddy 2010	HR for antepartum singleton SB (NHB v NHW)	X					unclear	2.00 (1.60, 2.40)
	HR for antepartum singleton SB, nullips (NHB v NHW)	X		X			unclear	1.9 (1.4, 2.6)
	HR for antepartum singleton SB, multiparous (NHB v NHW)	X		X			unclear	1.9 (1.4, 2.6)
Rosenstein 2014	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB						n/a	1.91
	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB, 37 wk		X				n/a	1.95
	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB, 38 wk		X				n/a	2.30
	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB, 39 wk		X				n/a	2.16
	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB, 40 wk		X				n/a	1.65
	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB, 41 wk		X				n/a	1.82
	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given wk, NHW and NHB, 42 wk		X				n/a	1.47
Rush 1972	# SBs "per 1000" but ns whether only LB (probably), W and B, non-smokers			X			n/a	0.88 (0.38, 2.00)
	# SBs "per 1000" but ns whether only LB (probably), W and B, smokers			X			n/a	1.63 (0.86, 3.09)
Salihu and Kinniburgh 2004	OR for SB, singletons (B v W)	X	X				age, parity, ed, smoking, PNC	2.90 (2.80, 3.00)
	OR for SB, twins (B v W)	X	X				"	1.3 (1.2, 1.4)
	OR for SB, triplets (B v W)	X	X				"	1.2 (0.7, 2.1)
	OR for SB (B v W)	X					age, parity, ed, marital, smoking, alcohol, PNC, birth order	0.80 (0.49, 1.30)
Salihu 2005	OR for SB in singletons (NHB v NHW singleton)	X					marital, age, ed, PNC, sex, plurality (by GEE)	3.0
Salihu 2006	OR for subsequent SB (prior C v vaginal)	X		X			age, parity, marital, ed, smoking, BMI, PNC, yr, preg comp	1.4
	OR for subsequent SB, 28-31 GA in this preg (prior C v vaginal)	X	X	X			"	1.18

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	OR for subsequent SB, 32-35 GA in this preg (prior C v vaginal)	X	X	X			"	2.0
	OR for subsequent SB, 35+ GA in this preg (prior C v vaginal)	X	X	X			"	1.4
Salihu 2007	HR for SB (W or B obese v W normal weight)	X		X			age, ed, marital, smoking, PNC, sex, yr	1.36
	HR for SB (W or B class I obese v W normal weight)	X		X			"	1.23
	HR for SB (W or B class II obese v W normal weight)	X		X			"	1.36
	HR for SB (W or B extreme obese v W normal weight)	X		X			"	1.28
Salihu 2009	OR for SB (underweight v normal weight)	X		X			age, parity, smoking, ed, marital, PNC, sex, yr, preg comp, PTB, SGA	1.29
	OR for early SB (underweight v normal weight)	X	X	X			"	1.00
	OR for late SB (underweight v normal weight)	X	X	X			"	1.17
Sapra 2017	% deliveries that were spontaneous terminations, NHW and NHB						n/a	0.78 (0.77, 0.80)
	% deliveries that were spontaneous terminations, NHW and NHB, <20 yrs			X			n/a	0.82 (0.76, 0.88)
	% deliveries that were spontaneous terminations, NHW and NHB, 20-24 yrs			X			n/a	0.89 (0.86, 0.93)
	% deliveries that were spontaneous terminations, NHW and NHB, 25-29 yrs			X			n/a	0.91 (0.88, 0.94)
	% deliveries that were spontaneous terminations, NHW and NHB, 30-34 yrs			X			n/a	0.96 (0.93, 0.99)
	% deliveries that were spontaneous terminations, NHW and NHB, 35+ yrs			X			n/a	0.94 (0.92, 0.96)
	% deliveries that were spontaneous terminations, NHW and NHB, married			X			n/a	0.71 (0.68, 0.74)
	% deliveries that were spontaneous terminations, NHW and NHB, unmarried/unknown status			X			n/a	0.39 (0.38, 0.40)
	% deliveries that were spontaneous terminations, NHW and NHB, US-born			X			n/a	0.75 (0.74, 0.76)
	% deliveries that were spontaneous terminations, NHW and NHB, foreign born/unknown status			X			n/a	0.80 (0.78, 0.81)
	% deliveries that were spontaneous terminations, NHW and NHB, nullips			X			n/a	0.83 (0.81, 0.84)
	% deliveries that were spontaneous terminations, NHW and NHB, parous			X			n/a	0.74 (0.73, 0.76)
	% deliveries that were spontaneous terminations, NHW and NHB, unknown parity			X			n/a	1.96 (1.92, 1.99)
	% deliveries that were spontaneous terminations, NHW and NHB, Medicaid			X			n/a	1.59 (1.46, 1.74)
	% deliveries that were spontaneous terminations, NHW and NHB, other insurance payer			X			n/a	1.27 (1.23, 1.32)
Schlenker 2009	average # FDs per 1000 TB, NHW and NHB, 2002–2007		X				n/a	2.15 (1.43, 3.22)
	average # FDs per 1000 TB, NHW and NHB, 1990–2001		X				n/a	2.55 (1.87, 3.47)
Schummers 2019	% births that were SBs, W and B						n/a	2.00 (1.97, 2.03)
	% births that were SBs, W and B, 15 yrs			X			n/a	1.60
	% births that were SBs, W and B, 20 yrs			X			n/a	1.83
	% births that were SBs, W and B, 25 yrs			X			n/a	2.50
	% births that were SBs, W and B, 30 yrs			X			n/a	2.86
	% births that were SBs, W and B, 35 yrs			X			n/a	2.67
	% births that were SBs, W and B, 40 yrs			X			n/a	2.50
	% births that were SBs, W and B, 45 yrs			X			n/a	2.50
Scott 1997	% hospitalizations for severe comp of preg that were for spontaneous abortions, W and B						n/a	1.5
Shahul 2015	OR for IUFD in those with preeclampsia (AA v W)	X					age, income, hospital (region, teaching status), mode of delivery, plurality, diab (with and without comp), yr, obesity, insurance	2.45 (2.14, 2.82)
Sharma 2006	OR for SB in second preg (prior SB v livebirth)	X		X			age, parity, marital, ed, smoking, BMI, PNC, IPI, yr	0.77
Singh 2018	% deliveries with antepartum FD (SB), NHW and NHB						n/a	2.67 (2.23, 3.19)
Tan 2004	RaR for FD (both parents B v W)	X					unadjusted	1.37 (1.26, 1.49)
	RaR for early FD (both parents B v W)	X	X				unadjusted	1.56 (1.40, 1.73)
	RaR for late FD (both parents B v W)	X	X				unadjusted	1.15 (1.01, 1.31)
Tanner 2018	# SBs per 1000 TB, NHW and NHB						n/a	1.27 (0.62, 2.62)
Timofeev 2014	OR for SB (AA v Caucasian)	X					unadjusted	4.60 (2.00, 10.40)
Tolcher 2020	RR for SB in low-risk population (aspirin v placebo)	X		X			unadjusted	3.44
	RR for SB in high-risk population (aspirin v placebo)	X		X			unadjusted	0.89

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
Tyler 2012	# FDs per 1,000 LB, NHW and NHB						n/a	2.28
	# FDs per 1,000 LB, NHW and NHB, Area 1 of the USA (FD registration includes all products of conception)			X			n/a	2.27
	# FDs per 1,000 LB, NHW and NHB, Area 2 of the USA (FD registration includes birthweight and gestational age criteria)			X			n/a	2.22
	# FDs per 1,000 LB, NHW and NHB, Area 3 of the USA (FD registration includes birthweight only criteria)			X			n/a	2.2
	# FDs per 1,000 LB, NHW and NHB, Area 4 of the USA (FD registration includes gestational age only criteria)			X			n/a	2.22
	# FDs per 1,000 LB, NHW and NHB, Area 1, 20-22 wk		X	X			n/a	0.9
	# FDs per 1,000 LB, NHW and NHB, Area 2, 20-22 wk		X	X			n/a	0.8
	# FDs per 1,000 LB, NHW and NHB, Area 3, 20-22 wk		X	X			n/a	0.4
	# FDs per 1,000 LB, NHW and NHB, Area 4, 20-22 wk		X	X			n/a	0.9
	# FDs per 1,000 LB, NHW and NHB, Area 1, 23-27 wk		X	X			n/a	0.8
	# FDs per 1,000 LB, NHW and NHB, Area 2, 23-27 wk		X	X			n/a	0.8
	# FDs per 1,000 LB, NHW and NHB, Area 3, 23-27 wk		X	X			n/a	0.9
	# FDs per 1,000 LB, NHW and NHB, Area 4, 23-27 wk		X	X			n/a	0.8
	# FDs per 1,000 LB, NHW and NHB, Area 1, 28-32 wk		X	X			n/a	1.2
	# FDs per 1,000 LB, NHW and NHB, Area 2, 28-32 wk		X	X			n/a	1.0
	# FDs per 1,000 LB, NHW and NHB, Area 3, 28-32 wk		X	X			n/a	1.1
	# FDs per 1,000 LB, NHW and NHB, Area 4, 28-32 wk		X	X			n/a	1.1
	# FDs per 1,000 LB, NHW and NHB, Area 1, 33-36 wk		X	X			n/a	1.3
	# FDs per 1,000 LB, NHW and NHB, Area 2, 33-36 wk		X	X			n/a	1.2
	# FDs per 1,000 LB, NHW and NHB, Area 3, 33-36 wk		X	X			n/a	1.5
	# FDs per 1,000 LB, NHW and NHB, Area 4, 33-36 wk		X	X			n/a	1.3
	# FDs per 1,000 LB, NHW and NHB, Area 1, 37+ wk		X	X			n/a	1.5
	# FDs per 1,000 LB, NHW and NHB, Area 2, 37+ wk		X	X			n/a	1.7
	# FDs per 1,000 LB, NHW and NHB, Area 3, 37+ wk		X	X			n/a	2.1
	# FDs per 1,000 LB, NHW and NHB, Area 4, 37+ wk		X	X			n/a	1.6
	# FDs per 1,000 LB, NHW and NHB, US, 20 wk, FAR approach		X	X			n/a	2.92
	# FDs per 1,000 LB, NHW and NHB, Area 3, 20 wk, FAR approach		X	X			n/a	1.55
	# FDs per 1,000 LB, NHW and NHB, US, 23 wk, FAR approach		X	X			n/a	2.56
	# FDs per 1,000 LB, NHW and NHB, Area 3, 23 wk, FAR approach		X	X			n/a	2.78
	# FDs per 1,000 LB, NHW and NHB, US, 28 wk, FAR approach		X	X			n/a	2.49
	# FDs per 1,000 LB, NHW and NHB, Area 3, 28 wk, FAR approach		X	X			n/a	2.32
	# FDs per 1,000 LB, NHW and NHB, US, 33 wk, FAR approach		X	X			n/a	1.96
	# FDs per 1,000 LB, NHW and NHB, Area 3, 33 wk, FAR approach		X	X			n/a	2.21
	# FDs per 1,000 LB, NHW and NHB, US, 37 wk, FAR approach		X	X			n/a	1.61
	# FDs per 1,000 LB, NHW and NHB, Area 3, 37 wk, FAR approach		X	X			n/a	2.07
Vintzileos 2002	RR for FD (PNC absent v present)	X			X		unclear	0.85
	RR for FD with mat anemia (PNC absent v present)	X		X	X		anemia, IP fever, preterm PROM, hydramnios, diab, chronic hyperten, preg induced hyperten, renal disease, placental abruption, placenta previa, bleeding unknown cause, FGR, post-term, prior PT/SGA, age, gravidity, marital, ed	2.72
	RR for FD with IP fever (PNC absent v present)	X		X	X		"	1.16
	RR for FD with preterm PROM (PNC absent v present)	X		X	X		"	1.24
	RR for FD with hydramnios (PNC absent v present)	X		X	X		"	2.67
	RR for FD with diab (PNC absent v present)	X		X	X		"	1.13
	RR for FD with chronic hypert (PNC absent v present)	X		X	X		"	1.07
	RR for FD with preg induced hypert (PNC absent v present)	X		X	X		"	0.98
	RR for FD with placental abruption (PNC absent v present)	X		X	X		"	1.80
	RR for FD with placenta previa (PNC absent v present)	X		X	X		"	1.02

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	RR for FD with bleeding unknown cause (PNC absent v present)	X		X	X		"	1.66
	RR for FD with FGR (PNC absent v present)	X	X		X		"	0.96
	RR for FD with post-term (PNC absent v present)	X	X		X		"	1.00
	RR for FD with prior PTB/SGA (PNC absent v present)	X		X	X		"	0.92
	RR for FD with none of anemia, IP fever, preterm PROM, hydramnios, diab, chronic hypert, preg induced hypert, renal disease, placental abruption, placenta previa, bleeding unknown cause, FGR, post-term, prior PTB/SGA (PNC absent v present)	X		X	X		"	0.96
Williams 2018	OR for SB (current low seg vs high, Dissimilarity Index)	X				X	age, yr, insurance, marital, smoking, alcohol, BMI, prior SB, SB risks in prior preg (prior C-section, prior PTB), current risks (SGA, PTB, placental abruption), preconception chronic disease (asthma, hyperten, diab), area-level % poverty, exposure to ozone, area temperature	0.30
	OR for SB (current moderate seg vs high, Dissimilarity Index)	X				X	"	1.55
	OR for SB (current low seg vs high, Isolation Index)	X				X	"	0.76
	OR for SB (current moderate seg vs high, Isolation Index)	X				X	"	0.58
	OR for SB (stay moderate seg vs stay high, Dissimilarity Index)	X				X	age, yr, insurance, marital, smoking, alcohol, BMI, prior SB, prior c-section, prior PTB, SGA, PTB, placental abruption, asthma, hyperten, diab, area-level % poverty, change in poverty from 1990 to birth yr, ozone, temperature	1.09
	OR for SB (stay low seg vs stay high, Dissimilarity Index)	X				X	"	0.34
	OR for SB (any decrease seg vs stay high, Dissimilarity Index)	X				X	"	0.71
	OR for SB (stay moderate seg vs stay high, Isolation Index)	X				X	"	0.62
	OR for SB (stay low seg vs stay high, Isolation Index)	X				X	"	1.17
	OR for SB (any decrease seg vs stay high, Isolation Index)	X				X	"	0.23
	OR for SB (any increase seg vs stay high, Isolation Index)	X				X	"	0.92
Willinger 2009	CH for SB at 20-41 wk (35+ v <35)	X		X			unadjusted	1.09
	CH for SB at 20-41 wk (12+ v <12 yr ed)	X		X			unadjusted	1.30
	CH for SB at 20-41 wk (1+ parity v 0)	X		X			unadjusted	1.03
	CH for SB, 20-23 wk (NHB v NHW)	X	X				unadjusted	2.75 (2.62, 2.88)
	CH for SB, 24-27 wk (NHB v NHW)	X	X				unadjusted	2.46 (2.30, 2.63)
	CH for SB, 28-31 wk (NHB v NHW)	X	X				unadjusted	2.67 (2.48, 2.88)
	CH for SB, 32-33 wk (NHB v NHW)	X	X				unadjusted	2.35 (2.11, 2.61)
	CH for SB, 34-36 wk (NHB v NHW)	X	X				unadjusted	1.84 (1.70, 2.00)
	CH for SB, 37-38 wk (NHB v NHW)	X	X				unadjusted	1.72 (1.57, 1.89)
	CH for SB, 39-40 wk (NHB v NHW)	X	X				unadjusted	1.57 (1.41, 1.75)
	CH for SB, 41 wk (NHB v NHW)	X	X				unadjusted	1.73 (1.40, 2.14)
	CH for SB, 20-41 wk (NHB v NHW)	X	X				unadjusted	2.20 (2.14, 2.26)
	RR of SB, <35 yr 20-27 wk (NHB v NHW)	X	X	X			unadjusted	2.70 (2.59, 2.81)
	RR of SB, <35 yr 28-36 wk (NHB v NHW)	X	X	X			unadjusted	2.25 (2.13, 2.37)
	RR of SB, <35 yr 37-41 wk (NHB v NHW)	X	X	X			unadjusted	1.63 (1.51, 1.75)
	RR of SB, <35 yr 20-41 wk (NHB v NHW)	X	X	X			unadjusted	2.22 (2.16, 2.29)
	RR of SB, 35+ yr 20-27 wk (NHB v NHW)	X	X	X			unadjusted	2.79 (2.53, 3.09)
	RR of SB, 35+ yr 28-36 wk (NHB v NHW)	X	X	X			unadjusted	2.89 (2.55, 3.27)
	RR of SB, 35+ yr 37-41 wk (NHB v NHW)	X	X	X			unadjusted	1.71 (1.43, 2.05)
	RR of SB, 35+ yr 20-41 wk (NHB v NHW)	X	X	X			unadjusted	2.43 (2.26, 2.61)
	RR of SB, ≤12 ed 20-27 wk (NHB v NHW)	X	X	X			unadjusted	2.16 (2.05, 2.28)
	RR of SB, ≤12 ed 28-36 wk (NHB v NHW)	X	X	X			unadjusted	1.89 (1.78, 2.02)
	RR of SB, ≤12 ed 37-41 wk (NHB v NHW)	X	X	X			unadjusted	1.35 (1.23, 1.47)
	RR of SB, ≤12 ed 20-41 wk (NHB v NHW)	X	X	X			unadjusted	1.82 (1.75, 1.89)
	RR of SB, 12+ ed 20-27 wk (NHB v NHW)	X	X	X			unadjusted	2.98 (2.79, 3.18)
	RR of SB, 12+ ed 28-36 wk (NHB v NHW)	X	X	X			unadjusted	2.29 (2.10, 2.51)
	RR of SB, 12+ ed 37-41 wk (NHB v NHW)	X	X	X			unadjusted	1.57 (1.39, 1.78)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	RR of SB, 12+ ed 20-41 wk (NHB v NHW)	X	X	X			unadjusted	2.36 (2.26, 2.48)
	RR of SB, 0 parity 20-27 wk (NHB v NHW)	X	X	X			unadjusted	2.77 (2.64, 2.90)
	RR of SB, 0 parity 28-36 wk (NHB v NHW)	X	X	X			unadjusted	2.25 (2.12, 2.40)
	RR of SB, 0 parity 37-41 wk (NHB v NHW)	X	X	X			unadjusted	1.60 (1.47, 1.75)
	RR of SB, 0 parity 20-41 wk (NHB v NHW)	X	X	X			unadjusted	2.25 (2.18, 2.33)
	RR of SB, 1+ parity 20-27 wk (NHB v NHW)	X	X	X			unadjusted	2.65 (2.47, 2.84)
	RR of SB, 1+ parity 28-36 wk (NHB v NHW)	X	X	X			unadjusted	2.48 (2.28, 2.69)
	RR of SB, 1+ parity 37-41 wk (NHB v NHW)	X	X	X			unadjusted	1.74 (1.55, 1.94)
	RR of SB, 1+ parity 20-41 wk (NHB v NHW)	X	X	X			unadjusted	2.28 (2.17, 2.39)
Wingate 2006	OR for FD (NHB v NHW)	X					marital, age, ed, parity, PNC, smoking, diab, hyperten, birthweight	1.01 (0.98, 1.04)
Wingate 2011	# FDs per 1,000 TB, NHW and NHB, 2001-2002		X				n/a	2.36 (2.30, 2.42)
	# FDs per 1,000 TB, NHW and NHB, 1990-1991		X				n/a	2.17 (2.12, 2.22)
	# FDs per 1,000 TB, NHW and NHB, 20-21 wk, 1990-1991		X				n/a	0.80 (0.80, 0.80)
	# FDs per 1,000 TB, NHW and NHB, 22-23 wk, 1990-1991		X				n/a	0.74 (0.74, 0.74)
	# FDs per 1,000 TB, NHW and NHB, 24-25 wk, 1990-1991		X				n/a	0.70 (0.70, 0.70)
	# FDs per 1,000 TB, NHW and NHB, 26-27 wk, 1990-1991		X				n/a	0.73 (0.73, 0.74)
	# FDs per 1,000 TB, NHW and NHB, 28-29 wk, 1990-1991		X				n/a	0.74 (0.73, 0.74)
	# FDs per 1,000 TB, NHW and NHB, 30-31 wk, 1990-1991		X				n/a	0.74 (0.73, 0.75)
	# FDs per 1,000 TB, NHW and NHB, 32-33 wk, 1990-1991		X				n/a	0.75 (0.74, 0.76)
	# FDs per 1,000 TB, NHW and NHB, 34-35 wk, 1990-1991		X				n/a	0.85 (0.83, 0.87)
	# FDs per 1,000 TB, NHW and NHB, 36-37 wk, 1990-1991		X				n/a	1.08 (1.05, 1.11)
	# FDs per 1,000 TB, NHW and NHB, 38-39 wk, 1990-1991		X				n/a	1.44 (1.37, 1.50)
	# FDs per 1,000 TB, NHW and NHB, 40-41 wk, 1990-1991		X				n/a	1.54 (1.46, 1.62)
	# FDs per 1,000 TB, NHW and NHB, 42-43 wk, 1990-1991		X				n/a	1.53 (1.47, 1.61)
	# FDs per 1,000 TB, NHW and NHB, 44+ wk, 1990-1991		X				n/a	1.02 (0.97, 1.08)
	# FDs per 1,000 TB, NHW and NHB, 20-21 wk, 2001-2002		X				n/a	0.90 (0.89, 0.90)
	# FDs per 1,000 TB, NHW and NHB, 22-23 wk, 2001-2002		X				n/a	0.79 (0.79, 0.80)
	# FDs per 1,000 TB, NHW and NHB, 24-25 wk, 2001-2002		X				n/a	0.71 (0.71, 0.72)
	# FDs per 1,000 TB, NHW and NHB, 26-27 wk, 2001-2002		X				n/a	0.84 (0.83, 0.84)
	# FDs per 1,000 TB, NHW and NHB, 28-29 wk, 2001-2002		X				n/a	0.95 (0.95, 0.96)
	# FDs per 1,000 TB, NHW and NHB, 30-31 wk, 2001-2002		X				n/a	0.98 (0.98, 0.99)
	# FDs per 1,000 TB, NHW and NHB, 32-33 wk, 2001-2002		X				n/a	1.04 (1.03, 1.05)
	# FDs per 1,000 TB, NHW and NHB, 34-35 wk, 2001-2002		X				n/a	1.15 (1.13, 1.18)
	# FDs per 1,000 TB, NHW and NHB, 36-37 wk, 2001-2002		X				n/a	1.28 (1.24, 1.32)
	# FDs per 1,000 TB, NHW and NHB, 38-39 wk, 2001-2002		X				n/a	1.63 (1.54, 1.72)
	# FDs per 1,000 TB, NHW and NHB, 40-41 wk, 2001-2002		X				n/a	1.56 (1.47, 1.66)
	# FDs per 1,000 TB, NHW and NHB, 42-43 wk, 2001-2002		X				n/a	1.77 (1.68, 1.86)
	# FDs per 1,000 TB, NHW and NHB, 44+ wk, 2001-2002		X				n/a	1.69 (1.61, 1.78)
Wingate 2012	OR for FD (2001-2002 vs 1995-1996)	X	X				age, marital, ed, parity, smoking, diab, hyperten disorders, PNC	1.03
	OR for FD in smoker 1995-1996 (NHB v W)	X	X	X			marital, age, ed, parity, PNC, diab, hyperten disorders	2.43 (2.19, 2.69)
	OR for FD in smoker 2001-2002 (NHB v W)	X	X	X			"	2.33 (2.09, 2.59)
	OR for FD with diab 1995-1996 (NHB v W)	X	X	X			marital, age, ed, parity, PNC, smoking, hyperten disorders	2.40 (1.97, 2.93)
	OR for FD with diab 2001-2002 (NHB v W)	X	X	X			"	2.51 (2.09, 3.01)
	OR for FD with hyperten disorders 1995-1996 (NHB v W)	X	X	X			marital, age, ed, parity, PNC, smoking, diab	2.90 (2.47, 3.41)
	OR for FD with hyperten disorders 2001-2002 (NHB v W)	X	X	X			"	3.05 (2.62, 3.55)
Wingate 2015	OR for FM (2005-2008 vs 1995-1998)	X	X				marital, age, parity, diab, hyperten disorders	1.03
	OR for early FM (20-27 wk) (2005-2008 vs 1995-1998)	X	X				"	0.94
	OR for late FM (28+ wk) (2005-2008 vs 1995-1998)	X	X				"	1.08
Wingate 2017	PRaR for FM (NHB v NHW)	X					yr, age, diab, hyperten disorders	2.01 (1.97, 2.05)

Report	Estimate (exposure, if any)	Domains of analysis [a]					Adjusted for	SDR (95% CI)
		R	F	M	H	S		
	PRaR for FM 22-23 wk (NHB v NHW)	X	X				"	0.76 (0.71, 0.81)
	PRaR for FM 24-25 wk (NHB v NHW)	X	X				"	0.70 (0.65, 0.75)
	PRaR for FM 26-27 wk (NHB v NHW)	X	X				"	0.83 (0.77, 0.88)
	PRaR for FM 28-29 wk (NHB v NHW)	X	X				"	0.97 (0.91, 1.04)
	PRaR for FM 30-31 wk (NHB v NHW)	X	X				"	0.99 (0.93, 1.06)
	PRaR for FM 32-33 wk (NHB v NHW)	X	X				"	1.11 (1.04, 1.18)
	PRaR for FM 34-35 wk (NHB v NHW)	X	X				"	1.18 (1.12, 1.26)
	PRaR for FM 36-37 wk (NHB v NHW)	X	X				"	1.37 (1.29, 1.44)
	PRaR for FM 38-39 wk (NHB v NHW)	X	X				"	1.58 (1.50, 1.67)
	PRaR for FM 40-41 wk (NHB v NHW)	X	X				"	1.51 (1.39, 1.65)
	PRaR for FM 42-43 wk (NHB v NHW)	X	X				"	1.68 (1.45, 1.95)
Witt 2012	OR for non-live birth (excluding abortions) (NHB v NHW)	X					preconception mental health, age, marital, ed, insurance, income, # children in household	0.73 (0.49, 1.08)
Xu 2009	risk ratio for FD (NHB v NHW)	X					unadjusted	1.78 (1.48, 2.13)
Yankauer 1950	# FDs per 1000 livebirths, W and non-W/Negro						n/a	1.77 (1.73, 1.82)
	# FDs per 1000 livebirths, W and non-W/Negro, < 5% of births non-W in health area					X	n/a	1.48 (1.33, 1.64)
	# FDs per 1000 livebirths, W and non-W/Negro, 5-9% of births non-W in health area					X	n/a	1.46 (1.29, 1.66)
	# FDs per 1000 livebirths, W and non-W/Negro, 10-24% of births non-W in health area					X	n/a	1.61 (1.48, 1.76)
	# FDs per 1000 livebirths, W and non-W/Negro, 25-49% of births non-W in health area					X	n/a	1.52 (1.39, 1.66)
	# FDs per 1000 livebirths, W and non-W/Negro, 50-74% of births non-W in health area					X	n/a	1.37 (1.24, 1.51)
	# FDs per 1000 livebirths, W and non-W/Negro, 75%+ of births non-W in health area					X	n/a	1.43 (1.23, 1.66)
Yankauer 1958	# FDs per 1000 LB, W and non-W/Negro, 1953-1955		X				n/a	1.95 (1.92, 1.99)
	# FDs per 1000 LB, W and non-W/Negro, 1945-1947		X				n/a	1.77 (1.73, 1.82)
Yuan 2005	RaR for FD at wk 40-43 (1997 v 1991)	X	X				induction	0.68
	RaR for FD at wk 40-43, low-risk preg (1997 v 1991)	X	X	X			induction	0.53
	RaR for FD at wk 40-43, high-risk preg (1997 v 1991)	X	X	X			induction	0.80
Zhang 2013	OR for FD (AA v W)	X					age, state, yr, length of inpatient hospital stay, C-section	1.89 (1.81, 1.98)

Abbreviations: AA, African American; antihyperten, antihypertensive; AP, antepartum; ART, assisted reproductive technology; B, Black; BMI, body mass index; BW, birthweight; C, Cesarean section; CA, congenital anomaly; CH, cumulative hazard; characs, characteristics; CI, confidence interval; COD, cause of death; comp, complication; cond, condition; cty, County; diab, diabetes; ed, education; F, female; FAR, fetuses-at-risk; FD, fetal death; FGR, fetal growth restriction; FM, fetal mortality; GA, gestational age; GEE, generalized estimating equations; gest, gestational; HR, hazard ratio; HS, high school; hypert, hypertension; hyperten, hypertensive; ID, infant death; IDD, intellectual or developmental disability; IP, intrapartum; IPI, interpregnancy interval; IQR, interquartile range; IUFD, intrauterine fetal demise; LB, livebirth; LBW, low birthweight; M, male; marital, marital status; mat, maternal; mat cond, maternal condition; med, medication; met, metropolitan; multi, multiparity; multips, multiparous; NHAA, non-Hispanic African American; NHB, non-Hispanic Black; NHW, non-Hispanic white; NND, neonatal death; nonmet, non-metropolitan; ns, not stated; nulli, nulliparity; nullips, nulliparous; NW, non-white; OR, odds ratio; payer, healthcare payer status; par, parity; PNC, prenatal care; PR, prevalence ratio; PRaR, prevalence rate ratio; preg, pregnancy; preg comp, pregnancy complications; pregest, pregestational; pre-preg diab, pre-pregnancy diabetes; PROM, premature rupture of membranes; PT, preterm; PTB, preterm birth; RaR, rate ratio; RR, relative risk; SB, stillbirth; seg, segregation; SGA, small for gestational age; SLE, systemic lupus erythematosus; sociodem, sociodemographic; TB, total births; tri, trimester; W, white; wk, week; yr, year.

[a] *Domains of analysis are R, race; F, fetal; M, maternal; H, healthcare system; S, structural.*

Table A11: Stillbirth Disparity Ratios (95% CIs) for comparisons between Hispanic, Asian/Pacific Islander, American Indian/Alaska Native, and other racial/ethnic minority groups and white births (n = 112 SDRs from 51 reports)

Report	Estimate (exposure, if any)	Adjusted for	SDR (95% CI)
Hispanic			
Hispanic (no subgroup identified)			
Akobirshoev 2019	OR for SB (H v NHW with IDD)	age, insurance, median household income for zip code, co-morbidities, hospital (location, teaching status, bed number, region), year	2.53 (1.08, 5.92)
Barfield 2004	# FDs per 1000 total births, 2000, H and NHW	n/a	1.09
Brown 2007	OR for FD (H v W)	age, residence, comorbidity, substance abuse, psychologic abnormality, length of hospital stay, total hospital charges	0.76 (0.42, 1.37)
Cai, Hoff and Archer 2007	# FDs over FDs and live births per 1000, H and W	n/a	0.93 (0.53, 1.61)
Carmichael 2015	relative risk for SB in multiparous term (37-41 week) births (for every 1 unit increase in BMI), H and NHW	age, education, height	0.91
Carmichael 2019	OR for SB at 20-25 weeks (H v NHW singleton livebirth full-term)	education, payer, country of birth, BMI, smoking, pre-pregnancy diabetes and hypertension, parity, IPI, prior SB or PTB	1.11 (1.01, 1.23)
Clowse 2016	OR for SB (H v W with SLE)	age, insurance, thrombophilia, anemia, thrombocytopenia, drug use, alcohol use, tobacco use, chronic hypertension, chronic renal failure, diabetes, thyroid disorders, asthma, history of myocardial infarction, plurality, mode of delivery, placenta previa	1.34 (0.88, 2.01)
Creanga 2017	% pregnancy-related deaths, H and NHW	n/a	0.91 (0.51, 1.60)
Faiz 2012	HR for SB (H v NHW)	maternal characteristics, pregnancy complications	1.20 (1.10, 1.30)
Gregory 2003	relative risk for intrauterine fetal distress (35+ v <35, H v W)	unadjusted	1.38
Gregory 2014	# FDs per 1000 total births, 2012, H v NHW	n/a	1.09
Guendelman 1994	OR for FD (Hispanic with no history of FD vs NHW with no history of FD)	unclear	0.83
Healy 2006	OR for fetal demise 24+ weeks (H v W)	age, education, marital status, BMI, smoking, drug use, alcohol use, medication during pregnancy, pregestational diabetes, obstetric history (prior live birth, miscarriage, PTB), ART, antihypertensive medication use prior to pregnancy, site	1.60 (0.80, 2.90)
Kallan 2001	# FDs per 1000 total births, native-born only, H v NHW	n/a	1.56 (1.37, 1.77)
Larkin 2018	# intrauterine FDs per 1000, H v NHW	n/a	1.11 (1.09, 1.13)
Lorch 2012	OR for FD (H v NHW)	unadjusted	1.37 (1.28, 1.47)
MacDorman and Hoyert 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, H v NHW	n/a	1.10 (1.07, 1.14)
Rammah 2019	HR for SB (per IQR increase in ozone), H v NHW	unadjusted	1.07
Reddy 2010	HR for antepartum singleton SB (H v NHW)	unclear	1.50 (1.20, 1.90)
Rosenstein 2014	# SBs at that GA per 10,000 ongoing pregnancies minus half of the births in the given week, H v NHW	n/a	1.16
Salihu 2005	OR for SB in singletons (H v NHW singletons)	marital status, age, education, PNC, sex, plurality (by GEE)	0.91 (0.90, 0.92)
Scott 1997	% hospitalizations for severe complications of pregnancy that were for spontaneous abortions, H v W	n/a	1
Shahul 2015	OR for IUFD (H v W with preeclampsia)	age, income, hospital (region, teaching status), mode of delivery, plurality, diabetes (with and without complications), year, obesity, insurance	0.96 (0.82, 1.13)
Singh 2018	% deliveries with antepartum FD (SB), H v NHW	n/a	1.33 (1.06, 1.68)
Tanner 2018	# SBs per total births, NHW and H	n/a	1.03 (0.63, 1.69)

Report	Estimate (exposure, if any)	Adjusted for	SDR (95% CI)
Tolcher 2020	relative risk for SB (women receiving aspirin vs placebo in low-risk population), H v NHW	unadjusted	0.98
Willinger 2009	CH for SB between 20-41 weeks (35+ vs <35), H v NHW	unadjusted	1.2
Wingate 2006	OR for FD (H v NHW)	marital status, age, education, parity, PNC, smoking, diabetes, hypertension, birthweight	0.49 (0.47, 0.52)
Wingate 2011	# FDs at 20 weeks+ gestation per 1,000 live births plus FDs, 2001-2002, H v NHW	n/a	1.33 (1.30, 1.37)
Wingate 2015	OR for fetal mortality (2005-2008 vs 1995-1998), H v NHW	marital status, age, parity, diabetes, hypertensive disorders	1.57
Wingate 2017	prevalence rate ratio for FD (H v NHW)	year, age, diabetes, hypertensive disorders	1.09 (1.07, 1.11)
Witt 2012	OR for non-live birth (excluding abortions) (H v NHW)	preconception mental health, age, marital status, education, insurance, income, number of children in the household	0.60 (0.42, 0.86)
Zhang 2013	OR for FD (H v W)	age, state, year, length of inpatient hospital stay, C-section	0.86 (0.81, 0.92)
Puerto Rican			
Hoyert 1996	# FDs per 1,000 live births and FDs, NHW and PR	n/a	0.98 (0.81, 1.19)
MacDorman and Kirmeyer 2009b	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, W and PR	n/a	1.27 (1.15, 1.41)
MacDorman and Munson 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and PR	n/a	1.26 (1.13, 1.39)
MacDorman 2011	# FDs of 20 weeks of gestation or more per 1000 live births and FD, NHW and PR	n/a	1.3
MacDorman 2012	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and PR	n/a	1.27 (1.15, 1.40)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and PR	n/a	1.23 (1.11, 1.36)
Mexican			
Gould 2003	# FDs per 1000 total births, U.S.-born NHW and foreign-born Mexican American	n/a	1.15 (1.08, 1.23)
Hoyert 1996	# FDs per 1,000 live births and FDs, NHW and Mexican	n/a	1.05 (1.00, 1.10)
MacDorman and Kirmeyer 2009b	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, W and Mexican	n/a	1.09 (1.05, 1.14)
MacDorman and Munson 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and Mexican	n/a	1.02 (0.98, 1.06)
MacDorman 2011	# FDs of 20 weeks of gestation or more per 1000 live births and FD, NHW and Mexican	n/a	1.09
MacDorman 2012	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and Mexican	n/a	1.01 (0.97, 1.05)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and Mexican	n/a	1.05 (1.00, 1.09)
Cuban			
Hoyert 1996	# FDs per 1,000 live births and FDs, NHW and Cuban	n/a	1.15 (0.90, 1.47)
MacDorman and Kirmeyer 2009b	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, W and Cuban	n/a	0.87 (0.68, 1.10)
MacDorman and Munson 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and Cuban	n/a	1.10 (0.88, 1.36)
MacDorman 2011	# FDs of 20 weeks of gestation or more per 1000 live births and FD, NHW and Cuban	n/a	0.9
MacDorman 2012	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and Cuban	n/a	1.14 (0.93, 1.39)

Report	Estimate (exposure, if any)	Adjusted for	SDR (95% CI)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and Cuban	n/a	0.95 (0.77, 1.17)
Central/South American			
Hoyert 1996	# FDs per 1,000 live births and FDs, NHW and Central/S Am	n/a	0.90 (0.79, 1.02)
MacDorman and Kirmeyer 2009b	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, W and Central/S Am	n/a	0.94 (0.87, 1.01)
MacDorman and Munson 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and Central/S Am	n/a	0.92 (0.85, 0.99)
MacDorman 2011	# FDs of 20 weeks of gestation or more per 1000 live births and FD, NHW and Central/S Am	n/a	0.9
MacDorman 2012	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and Central/S Am	n/a	0.99 (0.92, 1.06)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and Central/S Am	n/a	0.93 (0.86, 1.01)
Other Hispanic			
Hoyert 1996	# FDs per 1,000 live births and FDs, NHW and Other H	n/a	1.93 (1.75, 2.14)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and O/unknown H	n/a	1.23 (1.15, 1.32)
Asian			
Asian (no subgroup identified)			
Cai, Hoff and Archer 2007	# FDs over FDs and live births per 1000, A and W	n/a	2.64 (1.15, 6.05)
Carmichael 2019	OR for SB at 20-25 weeks (A v NHW singleton livebirth full-term)	education, payer, country of birth, BMI, smoking, pre-pregnancy diabetes and hypertension, parity, IPI, prior SB or PTB	1.30 (1.13, 1.49)
Larkin 2018	# intrauterine FDs per 1000, W and NH A	n/a	0.88 (0.84, 0.92)
Lorch 2012	OR for FD (A v NHW)	unadjusted	1.18 (1.09, 1.28)
Reddy 2010	HR for antepartum singleton SB (A v NHW)	unclear	0.50 (0.30, 0.90)
Rosenstein 2014	# SBs at given GA per 10,000 ongoing pregnancies minus half of the births in the given week, NHW and A	n/a	1.02
Asian or Pacific Islander			
Barfield 2004	# FDs per 1000 total births, 2000, API and NHW	n/a	0.98
MacDorman and Hoyert 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and API	n/a	1.01
MacDorman and Kirmeyer 2009b	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, W and API	n/a	1.00 (0.94, 1.06)
MacDorman and Munson 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and API	n/a	0.96 (0.90, 1.02)
MacDorman 2011	# FDs of 20 weeks of gestation or more per 1000 live births and FD, NHW and API	n/a	1
MacDorman 2012	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and API	n/a	1.02 (0.96, 1.08)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and API	n/a	0.96 (0.90, 1.02)
Schummers 2019	% births that were SBs, W and API	n/a	0.86 (0.84, 0.88)
Scott 1997	% hospitalizations for severe complications of pregnancy that were for spontaneous abortions, W and API	n/a	0.5
Singh 2018	% deliveries with antepartum FD (SB), NHW and API	n/a	0.67 (0.38, 1.17)
Tanner 2018	# SBs per total births, NHW and A including PI/O	n/a	3.73 (2.57, 5.40)

Report	Estimate (exposure, if any)	Adjusted for	SDR (95% CI)
Indian			
Gould 2003	# FDs per 1000 total births, US-born NHW and foreign-born Asian Indian	n/a	1.69 (1.36, 2.10)
American Indian/Alaska Native			
Barfield 2004	# FDs per 1000 total births, 2000, AIAN and NHW	n/a	1.04
Buck 1995	# FDs per 1000 births (live births plus FDs 20 weeks or more), AI and W	n/a	0.97 (0.67, 1.41)
Larkin 2018	# intrauterine FDs per 1000, NHW and NH AN	n/a	1.22 (1.13, 1.32)
MacDorman and Hoyert 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and AIAN	n/a	1.23
MacDorman and Kirmeyer 2009b	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, W and AIAN	n/a	1.29 (1.14, 1.45)
MacDorman and Munson 2007	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs of 20 weeks or more, NHW and AIAN	n/a	1.17 (1.04, 1.33)
MacDorman 2011	# FDs of 20 weeks of gestation or more per 1000 live births and FD, NHW and AIAN	n/a	1.29
MacDorman 2012	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and AIAN	n/a	1.26 (1.12, 1.41)
MacDorman 2015	# FDs of 20 weeks of gestation or more per 1,000 live births and FDs at 20 weeks or more, NHW and AIAN	n/a	1.27 (1.13, 1.43)
Schummers 2019	% births that were SBs, W and AIAN	n/a	1.00 (0.94, 1.06)
Scott 1997	% hospitalizations for severe complications of pregnancy that were for spontaneous abortions, W and NA	n/a	0.5
Wingate 2015	OR for fetal mortality (2005-2008 vs 1995-1998), AIAN v NHW	marital status, age, parity, diabetes, hypertensive disorders	0.89
Wingate 2017	prevalence rate ratio for FD (AIAN v NHW)	year, age, diabetes, hypertensive disorders	1.29 (1.21, 1.37)
Other			
Getahun 2005	relative risk for SB (BW v WW)	age, education, paternal age, PNC, parity, marital status, smoking	1.37 (1.21, 1.54)
Getahun 2005	relative risk for SB (WB v WW)	age, education, paternal age, PNC, parity, marital status, smoking	1.17 (1.10, 1.26)
Gold 2010	OR for SB (BW v WW)	birthweight, GA, demographic factors, social, biological, and genetic/congenital risk factors, procedures	1.38 (0.76, 2.50)
Gold 2010	OR for SB (WB v WW)	birthweight, GA, demographic factors, social, biological, and genetic/congenital risk factors, procedures	1.35 (0.92, 1.98)
Tan 2004	rate ratio for FD (BW v WW)	unadjusted	0.87 (0.56, 1.36)
Tan 2004	rate ratio for FD (WB v WW)	unadjusted	1.17 (0.93, 1.48)
Cai, Hoff and Archer 2007	# FDs over FDs and live births per 1000, O and W	n/a	0.73 (0.18, 2.96)
Creanga 2017	% pregnancy-related deaths, O and NHW	n/a	0.92 (0.42, 2.00)
Faiz 2012	HR for SB (O v NHW)	maternal characteristics, pregnancy complications	0.80 (0.70, 1.00)
Gregory 2003	relative risk for intrauterine fetal distress (35+ v <35, O v W)	unadjusted	1.06
Healy 2006	OR for fetal demise 24+ weeks (O v W)	age, education, marital status, BMI, smoking, drug use, alcohol use, medication during pregnancy, pregestational diabetes, obstetric history (prior live birth, miscarriage, PTB), ART, antihypertensive medication use prior to pregnancy, site	1.70 (0.80, 3.80)
Hsieh 1997	# FDs per 1000 total births (FDs and live births), 1989-1990, W and O	n/a	0.92
Koonin 1997	% pregnancy-related maternal deaths with SB, W and O	n/a	0.91 (0.05, 15.95)
NCHS 1966	# FDs per 1,000 live births and FDs, W and non-W	n/a	1.95 (1.92, 1.98)
Reddy 2010	HR for antepartum singleton SB (O v NHW)	unclear	2.40 (1.80, 3.00)

Report	Estimate (exposure, if any)	Adjusted for	SDR (95% CI)
Shapiro 1965	# deaths of 20+ weeks and unknown GA per 1000 live births, W and non-W	n/a	1.92 (1.89, 1.95)
Singh 2018	% deliveries with antepartum FD (SB), NHW and O/multiracial	n/a	2.33 (1.57, 3.48)
Soffer 2018	% pregnancy outcomes that were IUFD, W and non-W	n/a	0
Tanner 2018	# SBs per total births, NHW and O	n/a	3.93 (2.14, 7.22)
U.S. Dept of Commerce 1936	# SBs per 100 live births, W and ”colored”	n/a	2.06 (2.10, 2.16)
Witt 2012	OR for non-live birth (excluding abortions) (O v NHW)	preconception mental health, age, marital status, education, insurance, income, number of children in the household	1.42 (0.81, 2.50)

Abbreviations: A, Asian, AI, American Indian, AIAN, American Indian/Alaska Native, API, Asian/Pacific Islander, ART, assisted reproductive technology, BMI, body mass index, BW, Black mother/white father, CH, cumulative hazard, FD, fetal death, GA, gestational age, GEE, generalized estimating equations, H, Hispanic, HR, hazard ratio, IDD, intellectual or developmental disability, IPI, inter-pregnancy interval, IQR, interquartile range, IUFD, intrauterine fetal death, NA, Native American, NH, non-Hispanic, NHW, non-Hispanic white, O, other racial/ethnic group, OR, odds ratio, PI, Pacific Islander, PNC, prenatal care, PR, Puerto Rican, PTB, preterm birth, S Am, South American, SB, stillbirth, SLE, systemic lupus erythematosus, W, white, WB, white mother/Black father, WW, white mother/white father.

Table A12: Summary of domains of analysis and explanation for 84 reports providing Black-white Stillbirth Disparity Ratios

Domain	Analysis		Explanation	
	# reports	%	# reports	%
Fetal	**39**	**46%**	**35**	**42%**
Gestational age	25	30%	22	26%
Year of birth	17	20%	0	-
Birthweight	10	12%	7	8%
Plurality	7	8%	4	5%
Sex	6	7%	0	-
Parity	6	7%	4	5%
Cause of death	3	4%	3	4%
Small for gestational age	3	4%	4	5%
Maternal	**30**	**36%**	**47**	**56%**
Age	15	18%	7	8%
Marital status	8	10%	1	1%
Adverse pregnancy outcomes	6	7%	2	2%
Pregnancy-related conditions	6	7%	11	13%
Maternal conditions	6	7%	23	27%
Weight	4	5%	8	10%
Education	3	4%	7	8%
Prenatal care	3	4%	13	15%
Health behaviors	3	4%	13	15%
Insurance	2	2%	4	5%
Nativity	2	2%	5	6%
Pregnancy-related knowledge, attitudes and practices	0	-	4	5%
Genetics	0	-	8	10%
General health	0	-	15	18%
Stress	0	-	21	25%
Family/community	**3**	**4%**	**17**	**20%**
Community	3	4%	10	12%
Families	0	-	5	6%
Socioeconomic status	0	-	7	8%
Healthcare	**0**	**-**	**32**	**38%**
Physicians	0	-	5	6%
Interventions	0	-	11	13%
Quality	0	-	19	23%
Access	0	-	19	23%
Structural	**4**	**5%**	**31**	**37%**
Racism	2	2%	17	20%
Other	2	2%	24	29%
Poverty	0	-	4	5%
Race [a]	37	44%	4	5%
None	**n/a**	**n/a**	**27**	**32%**

[a] *Race noted as a domain of analysis if used as an exposure in regression analyses; all other reports by definition used race as either a stratification factor or effect modifier.*

Table A13: Details of domains of analysis and explanation for 84 reports with data for Black-white Stillbirth Disparity Ratios (SDRs)

			Maternal														Fetal								Fam/Com			Healthcare				Structural			
	Race	Gen	Age	Ed	Mar	Wgt	Str	Nat	Hea	Mat	Prg	APO	Ins	PNC	KAP	Beh	GA	BW	SGA	COD	Par	Plu	Sex	Yr	Fam	SES	Com	Qual	Acc	Int	Dr	Rcm	Pov	Oth	None
Akobirshoev 2019																																			
analysis	X																																		
explanation						X			X	X					X													X	X		X				
Allen 2005																																			
analysis	X																																		
explanation							X			X				X		X	X														X				
Ananth 2005																																			
analysis	X																							X											
explanation																																			X
August 2011																																			
analysis	X											X																							
explanation																																			X
Barfield 1996																																			
analysis	X												X																						
explanation													X																						
Barfield 2004																																			
analysis																	X							X											
explanation																																			X
Brisendine 2020																																			
analysis	X		X														X																		
explanation		X	X				X			X						X									X		X				X				
Brown 2007																																			
analysis	X																																		
explanation									X																		X								
Brown 2012																																			
analysis	X																														X				
explanation							X																								X				
Buck 1995																																			
analysis			X							X	X							X	X																
explanation			X								X						X																X		
Cai, Hoff and Archer 2007																																			
analysis																		X									X								
explanation																																			X
Cai, Hoff and Okah 2007																																			
analysis	X																X	X																	
explanation		X															X	X																	
Carmichael 2015																																			
analysis						X											X				X														
explanation																	X				X							X							
Carmichael 2019																																			
analysis	X																X																		

			Maternal														Fetal								Fam/Com			Healthcare				Structural			
	Race	Gen	Age	Ed	Mar	Wgt	Str	Nat	Hea	Mat	Prg	APO	Ins	PNC	KAP	Beh	GA	BW	SGA	COD	Par	Plu	Sex	Yr	Fam	SES	Com	Qual	Acc	Int	Dr	Rcm	Pov	Oth	None
explanation																																		X
Clowse 2016																																		
analysis	X																																	
explanation																																		X
Creanga 2017																																		
analysis																																		
explanation																																		X
Demissie 2001																																		
analysis																								X										
explanation																																		X
Dryfhout 2010																																		
analysis	X																																	
explanation						X	X			X				X		X						X					X	X			X	X			
Dumas 2020																																		
analysis																																		
explanation																																		X
Faiz 2012																																		
analysis	X																																	
explanation				X						X	X			X		X																	X	
Getahun 2005																																		
analysis	X																																	
explanation		X	X		X									X		X									X								X	
Getahun 2007																																		
analysis	X		X	X	X	X				X	X	X		X		X	X		X	X	X		X											
explanation		X		X		X	X		X					X			X												X	X			X	
Gold 2010																																		
analysis	X																																	
explanation							X		X	X				X			X	X							X		X					X		X	
Gould 2003																																		
analysis																																		
explanation	X			X		X	X	X	X				X		X	X	X	X	X							X	X	X					X	
Grant 2017																																		
analysis																																		
explanation																																		X
Gregory 2003																																		
analysis			X																															
explanation																																		X
Gregory 2014																																		
analysis																	X							X										
explanation																																		X
Guendelman 1994																																		
analysis	X											X																						
explanation										X	X	X																X						
Healy 2006																																		
analysis	X																X																	
explanation							X	X							X	X												X		X				

			Maternal														Fetal								Fam/Com			Healthcare				Structural			
	Race	Gen	Age	Ed	Mar	Wgt	Str	Nat	Hea	Mat	Prg	APO	Ins	PNC	KAP	Beh	GA	BW	SGA	COD	Par	Plu	Sex	Yr	Fam	SES	Com	Qual	Acc	Int	Dr	Rcm	Pov	Oth	None
Hoyert 1996																																			
analysis			X	X	X									X			X				X						X								
explanation																																			X
Hsieh 1997																																			
analysis																		X						X											
explanation																		X				X													
Kallan 2001																																			
analysis								X																											
explanation								X																											
Koonin 1997																																			
analysis																																			
explanation																																			X
Kramer 2002																																			
analysis																																			
explanation																																			X
Larkin 2018																																			
analysis																																			
explanation																																			X
Lemon 2016																																			
analysis																																			
explanation						X																													
Lorch 2012																																			
analysis	X										X																								
explanation							X		X		X			X			X											X	X					X	
MacDorman and Hoyert 2007																																			
analysis			X		X												X	X				X	X												
explanation							X		X	X							X									X			X			X		X	
MacDorman and Munson 2007																																			
analysis			X		X												X	X				X	X	X											
explanation							X		X	X							X									X			X			X		X	
MacDorman and Kirmeyer 2009a																																			
analysis																																			
explanation									X	X							X												X						
MacDorman and Kirmeyer 2009b																																			
analysis			X		X												X	X				X	X	X											
explanation							X		X	X							X									X			X			X		X	
MacDorman 2011																																			
analysis																																			
explanation																	X											X						X	
MacDorman 2012																																			
analysis			X		X												X	X				X	X	X											
explanation							X		X	X							X									X			X			X		X	
MacDorman 2015																																			
analysis			X		X												X	X				X	X	X											
explanation							X		X	X							X												X			X		X	
Meyer 1999																																			

			Maternal														Fetal							Fam/Com			Healthcare				Structural			
	Race	Gen	Age	Ed	Mar	Wgt	Str	Nat	Hea	Mat	Prg	APO	Ins	PNC	KAP	Beh	GA	BW	SGA	COD	Par	Plu	Sex	Yr	Fam	SES	Com	Qual	Acc	Int	Dr	Rcm	Pov	Oth	None
analysis																						X		X											
explanation																						X													
Nabukera 2009																																			
analysis	X		X																																
explanation			X				X				X					X					X													X	
Powell-Griner 1989																																			
analysis																								X											
explanation																		X																	
Pruitt 2020																																			
analysis	X									X	X									X															
explanation							X		X											X						X		X	X		X				
Rammah 2019																																			
analysis																																		X	
explanation																																			X
Reddy 2010																																			
analysis	X																				X														
explanation																																			X
Rosenstein 2014																																			
analysis																	X																		
explanation				X							X		X			X		X											X	X				X	
Rush 1972																																			
analysis																X																			
explanation									X																									X	
Salihu and Kinniburgh 2004																																			
analysis	X																X	X				X													
explanation											X								X																
Salihu and Williams 2004																																			
analysis	X																																		
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Salihu 2005																																			
analysis	X																																		
explanation				X												X						X					X								
Salihu 2006																																			
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explanation	X	X								X	X	X			X													X			X				
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explanation						X				X										X								X							
Salihu 2009																																			
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explanation						X								X					X									X	X						
Sapra 2017																																			
analysis			X		X			X					X								X														
explanation																																			X
Schlenker 2009																																			
analysis																								X											

			Maternal														Fetal								Fam/Com			Healthcare				Structural			
	Race	Gen	Age	Ed	Mar	Wgt	Str	Nat	Hea	Mat	Prg	APO	Ins	PNC	KAP	Beh	GA	BW	SGA	COD	Par	Plu	Sex	Yr	Fam	SES	Com	Qual	Acc	Int	Dr	Rcm	Pov	Oth	None
explanation																																		X
Schummers 2019																																		
analysis			X																															
explanation			X				X																								X		X	
Scott 1997																																		
analysis																																		
explanation						X								X		X					X				X		X	X	X		X	X	X	
Shahul 2015																																		
analysis	X																																	
explanation		X								X	X															X			X	X	X				
Sharma 2006																																		
analysis												X																						
explanation																																		X
Singh 2018																																		
analysis																																		
explanation										X	X																		X					
Tan 2004																																		
analysis	X																X																	
explanation	X	X					X			X						X	X																X	
Tanner 2018																																		
analysis																																		
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Timofeev 2014																																		
analysis	X																																	
explanation																																		X
Tolcher 2020																																		
analysis											X																							
explanation																																		X
Tyler 2012																																		
analysis																	X										X							
explanation																	X															X	X	
Vintzileos 2002																																		
analysis										X	X	X		X			X		X	X														
explanation										X				X														X	X	X				
Williams 2018																																		
analysis																															X			
explanation							X																				X				X	X	X	
Willinger 2009																																		
analysis	X		X	X													X				X													
explanation			X	X				X	X	X	X						X		X	X	X						X			X				
Wingate 2006																																		
analysis	X																																	
explanation								X										X																
Wingate 2011																																		
analysis																	X							X										
explanation			X	X						X				X			X											X	X	X				

			Maternal														Fetal								Fam/Com			Healthcare				Structural			
	Race	Gen	Age	Ed	Mar	Wgt	Str	Nat	Hea	Mat	Prg	APO	Ins	PNC	KAP	Beh	GA	BW	SGA	COD	Par	Plu	Sex	Yr	Fam	SES	Com	Qual	Acc	Int	Dr	Rcm	Pov	Oth	None
Wingate 2012																																		
analysis	X									X						X								X										
explanation							X			X				X		X													X					
Wingate 2015																																		
analysis																	X							X										
explanation	X																X											X	X	X				X	
Wingate 2017																																		
analysis	X																X																	
explanation										X							X											X						X	
Witt 2012																																		
analysis	X																																	
explanation																																		X
Xu 2009																																		
analysis	X																																	
explanation																																		X
Yankauer 1950																																		
analysis																																	X	
explanation																									X		X	X			X			
Yankauer 1958																																		
analysis																								X										
explanation																															X			
Yuan 2005																																		
analysis	X		X							X							X							X										
explanation																	X												X					
Zhang 2013																																		
analysis	X																																	
explanation		X					X						X	X														X	X	X	X	X	X	X	

Domains are:

- *race;*
- *genetics (gen);*
- *maternal, including age, education (ed), marital (mar), weight (wgt), stress (str), nativity (nat), general health (hea), maternal conditions (mat), pregnancy-related conditions (prg), prior adverse pregnancy outcomes (APO), health insurance (ins), prenatal care (PNC), pregnancy-related knowledge, attitudes and practices (KAP), other health behaviors (beh);*
- *fetal, including gestational age (GA), birthweight (BW), small for gestational age (SGA), cause of death (COD), parity (par), plurality (plu), sex, birth year (yr);*
- *family and community, including family characteristics (fam), socioeconomic characteristics (SES), community characteristics (com);*
- *healthcare, including quality (qual), access (acc), interventions (int), physician-related characteristics (dr);*
- *structural, including racism (rcm), poverty (pov), other structural characteristics (oth).*

"None" indicates that no comments on racial disparity in stillbirth rates were found. See Table A2 for details of what each domain and category includes.

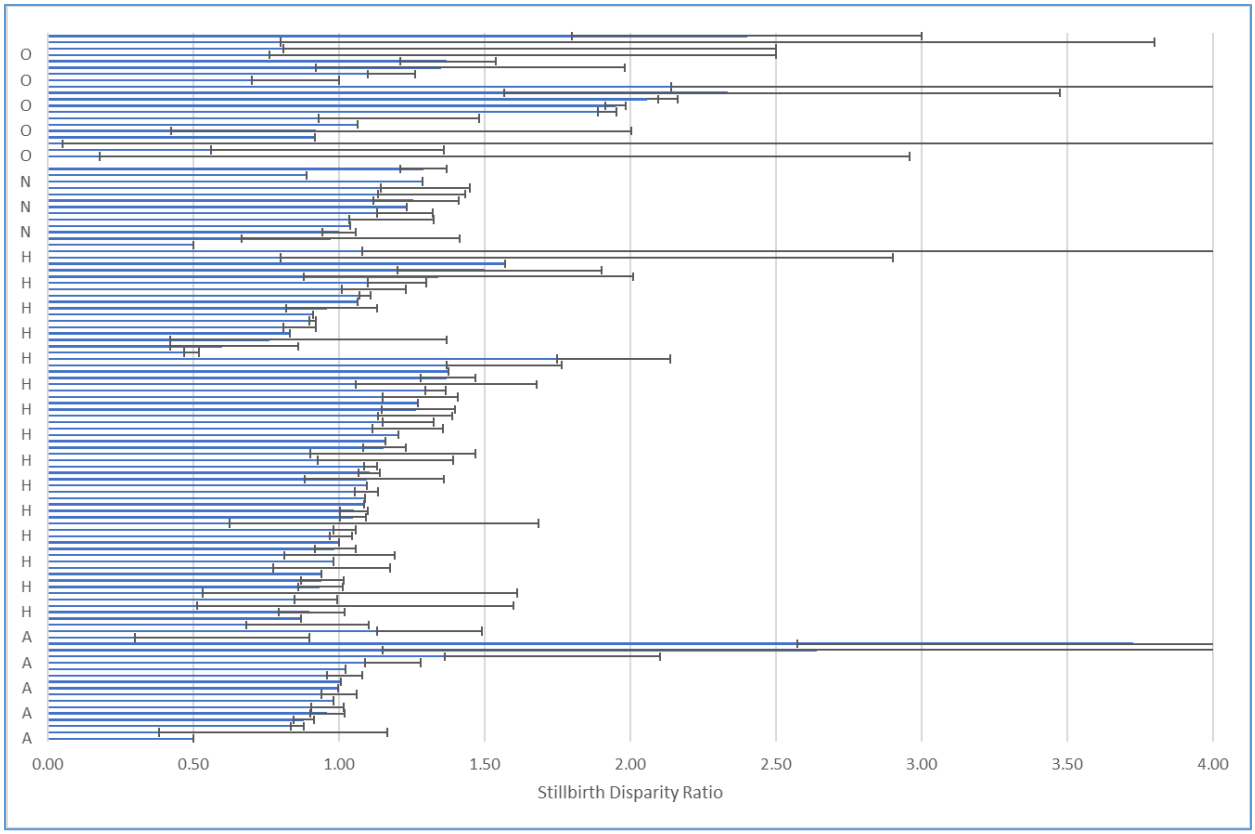


Figure A1: Stillbirth Disparity Ratios (SDRs) for racial/ethnic groups other than Black, 112 SDRs from 51 reports

Top to bottom*: O, Other (adjusted, unadjusted); N, Native American (adjusted, unadjusted); H, Hispanic (adjusted, unadjusted); A, Asian (adjusted, unadjusted).*

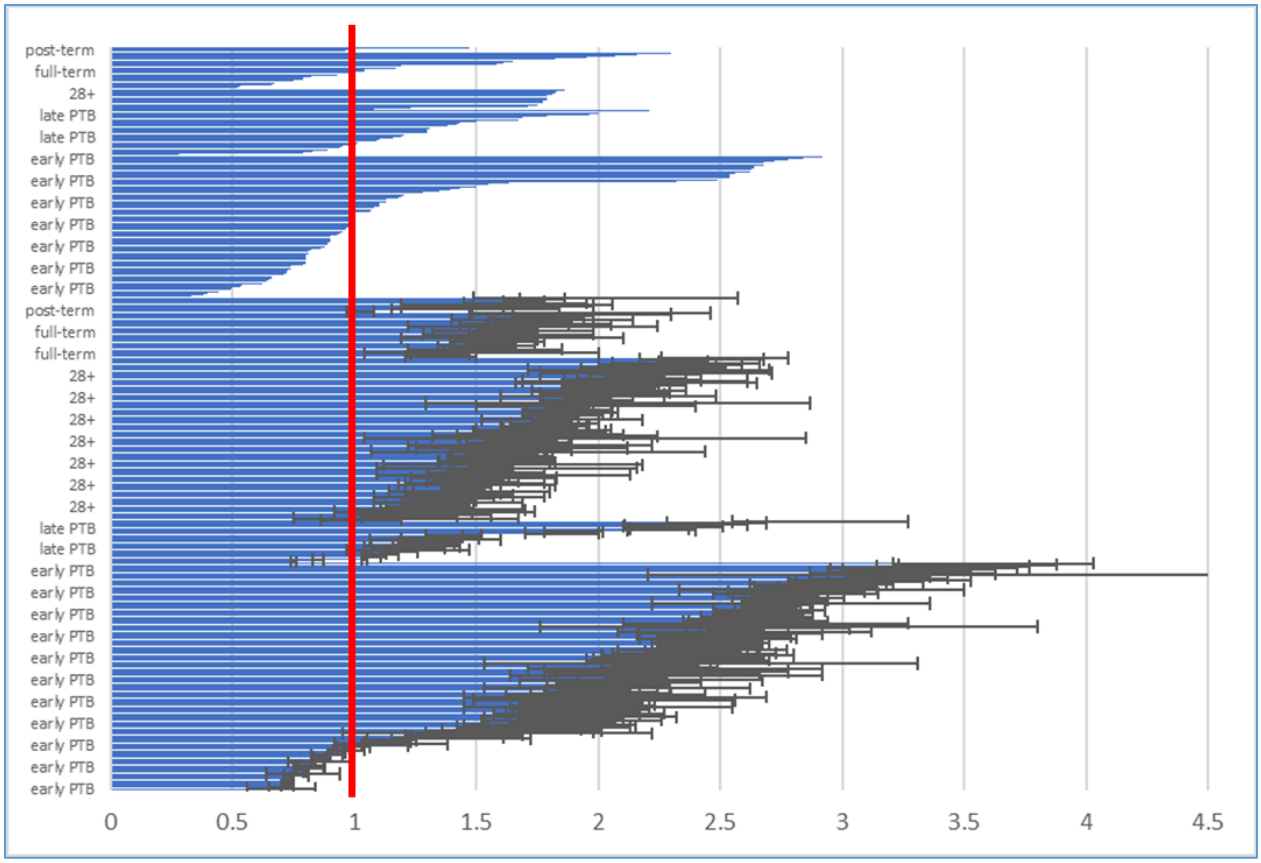


Figure A2: 445 Black-white SDRs that used gestational age as a category of analysis, ordered by gestational age at birth: (top) n=150 SDRs without 95% CIs from 8 reports; (bottom) n=295 SDRs with 95% CIs from 13 reports

Abbreviations: CI, confidence interval; SDR, Stillbirth Disparity Ratio.
Red line indicates null value of 1. SDRs whose 95% CI bars are entirely to the left of the red line, or blue bars ending to the left of the red line (for SDRs without 95% CIs) indicate greater risk of stillbirth in white than Black births; those with 95% CI bars entirely to the right of the red line, or blue bars ending to the right of the red line (for SDRs without 95% CIs), indicate greater risk of stillbirth in Black than white births; those with 95% CI bars crossing the red line indicate no evidence of significant difference in Black and white stillbirth risk at α=5%.
Subcategories for gestational age were:

- *Early preterm (including 20-27, 25-29, 28-32 weeks)*
- *Late preterm (including 33-36, 28-36, 30-34, 32-33, 32-35, 32-36, 35-39, 36-37 weeks)*
- *Full term (including 37-38, 39-40, 41, 38-39, 37-41, 37-39, 40-41 weeks)*
- *Post-term (including 42+ weeks)*
- *28+ weeks*

24 SDRs using gestational age as a domain of analysis were not included here due to gestational ages that aligned poorly with our categories (20-41, early, late, 24+, 35+, 37+, 40-43 weeks, as these overlap with other categories; e.g., 24+ weeks overlaps with early and late PTB as well as full-term and post-term).

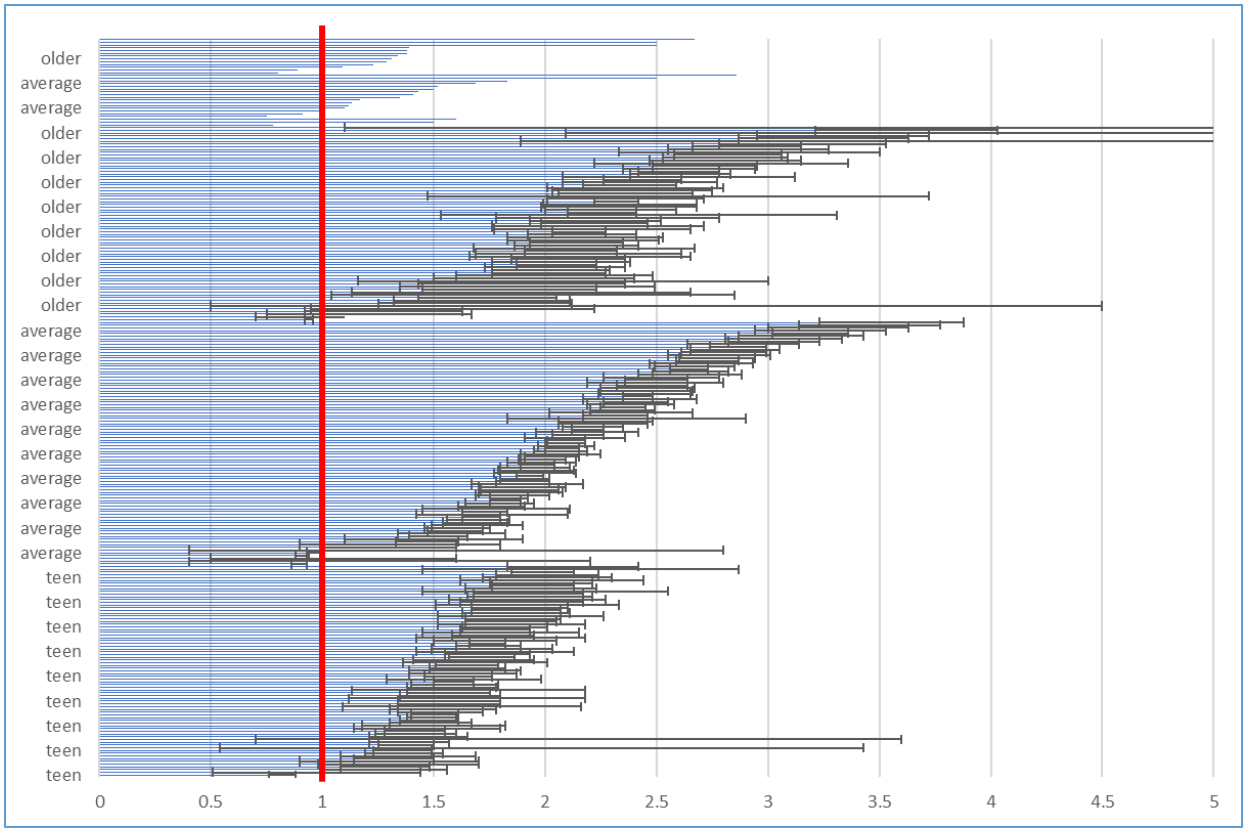


Figure A3: 269 Black-white SDRs that used maternal age as a category of analysis, ordered by maternal age at birth: (top) n=32 SDRs without 95% CIs from 5 reports; (bottom) n=237 SDRs with 95% CIs from 11 reports

Abbreviations: CI, confidence interval; SDR, Stillbirth Disparity Ratio.
Red line indicates null value of 1. SDRs whose 95% CI bars are entirely to the left of the red line, or blue bars ending to the left of the red line (for SDRs without 95% CIs) indicate greater risk of stillbirth in white than Black births; those with 95% CI bars entirely to the right of the red line, or blue bars ending to the right of the red line (for SDRs without 95% CIs), indicate greater risk of stillbirth in Black than white births; those with 95% CI bars crossing the red line indicate no evidence of significant difference in Black and white stillbirth risk at α=5%.
Subcategories for maternal age were:

- *Teen (including <20 years)*
- *Average (including 20-24, 25-29, 30-34, 20-29, 20-34 years)*
- *Older (including 35-39, 35+, 40+ years)*

4 SDRs using maternal age as a domain of analysis were not included here due to maternal age category that aligned poorly with our categories (<35 which overlaps with teen and average-aged mothers).

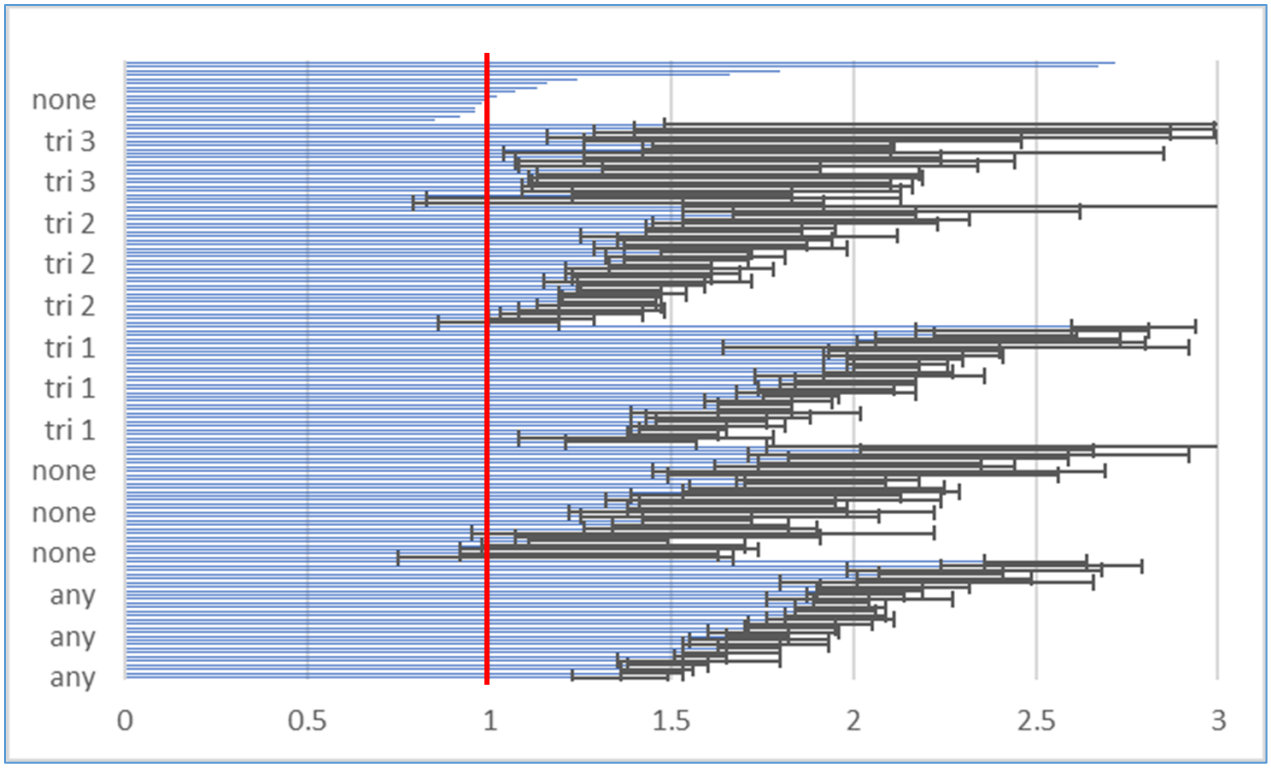


Figure A4: 150 Black-white SDRs with 95% CIs that used prenatal care as a category of analysis, ordered by trimester when care started and any/no prenatal care: (top) n=15 SDRs without 95% CIs from one report; (bottom) n=135 SDRs with 95% CIs from one report

Abbreviations: CI, confidence interval; SDR, Stillbirth Disparity Ratio; tri, trimester.
Red line indicates null value of 1. SDRs whose 95% CI bars are entirely to the left of the red line, or blue bars ending to the left of the red line (for SDRs without 95% CIs) indicate greater risk of stillbirth in white than Black births; those with 95% CI bars entirely to the right of the red line, or blue bars ending to the right of the red line (for SDRs without 95% CIs), indicate greater risk of stillbirth in Black than white births; those with 95% CI bars crossing the red line indicate no evidence of significant difference in Black and white stillbirth risk at α=5%.
Subcategories for PNC were:

- *Trimester 1 start*
- *Trimester 2 start*
- *Trimester 3 start*
- *Any PNC*
- *No PNC*

4 SDRs using PNC as a domain of analysis were not included here due to category that aligned poorly with our categories (late/no PNC which overlaps with tri 3 start and no PNC).

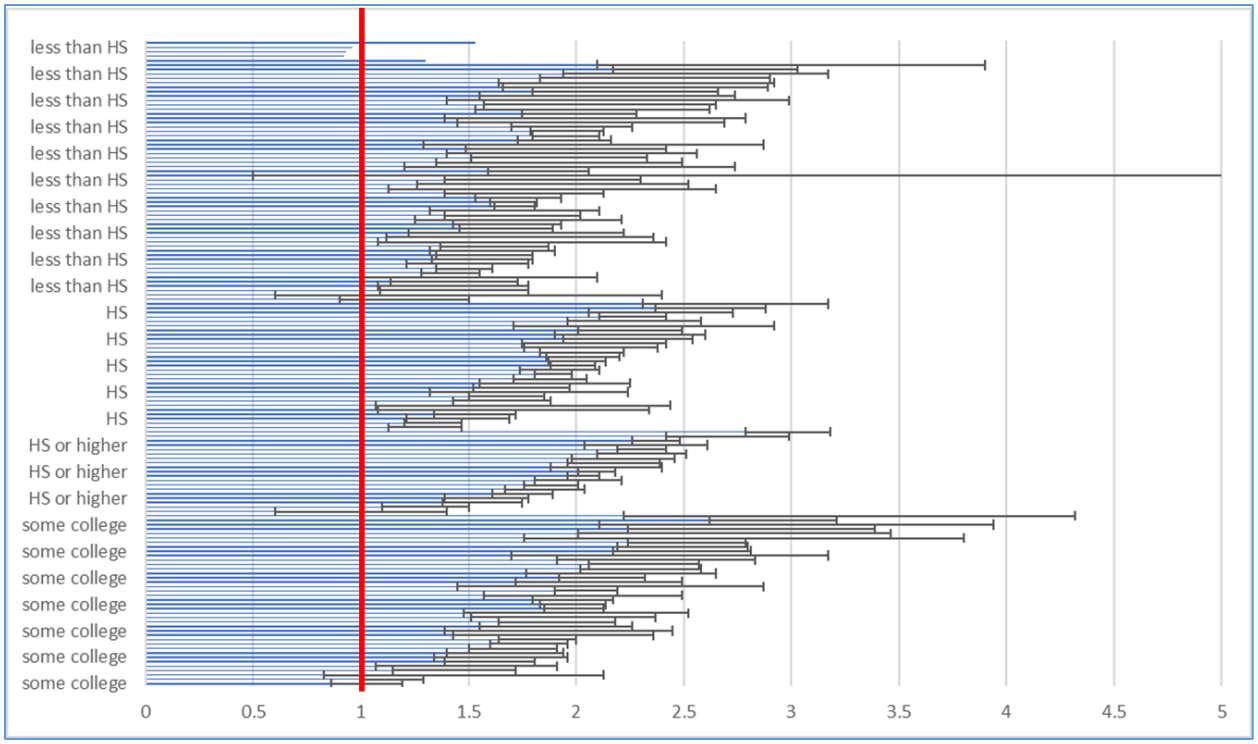


Figure A5: 146 Black-white SDRs that used maternal education as a category of analysis, ordered by number of years of education completed: (top) n=5 SDRs without 95% CIs from 2 reports; (bottom) n=141 SDRs with 95% CIs from 3 reports

Abbreviations: CI, confidence interval; SDR, Stillbirth Disparity Ratio.
Red line indicates null value of 1. SDRs whose 95% CI bars are entirely to the left of the red line, or blue bars ending to the left of the red line (for SDRs without 95% CIs) indicate greater risk of stillbirth in white than Black births; those with 95% CI bars entirely to the right of the red line, or blue bars ending to the right of the red line (for SDRs without 95% CIs), indicate greater risk of stillbirth in Black than white births; those with 95% CI bars crossing the red line indicate no evidence of significant difference in Black and white stillbirth risk at α=5%.
Subcategories for education were:

- *Some college (including 16+, 13-15, and 13+ years)*
- *Less than high school (including 0-8, <8, <12, 9-11, and 8-11 years)*
- *High school (including 12 years)*
- *High school or higher (including 12+ years)*

4 SDRs using education as a domain of analysis were not included here due to category that aligned poorly with our categories (≤12 which overlaps with high school and less than high school).

Additional tables and figures for Chapter 3

Table A14: Four structural racism measures: Formulas and data sources

Use	Formula	Variable definitions	Range and interpretation	Coding	ACS data sources
Index of Dissimilarity					
Main analyses[64 221 419-421]	$\frac{1}{2}\sum_{i=1}^{n}\left\lvert\frac{w_i}{W_T}-\frac{b_i}{B_T}\right\rvert$	w_i is the number of white and b_i the number of Black individuals in the i^{th} of n census tracts; W_T and B_T are the totals of these individuals in all census tracts of one PUMA	Assesses whether populations of minority and majority groups are evenly distributed across neighborhoods; range 0 (not segregated) to 1 (completely segregated)	Tertiles (tertile 3 = greatest segregation)[64]	Table B03002, "Hispanic or Latino Origin by Race", for vintages 2013 and 2018
Sensitivity analyses[212 227]	$\frac{\sum_{i=1}^{n}[t_i\lvert(p_i-P)\rvert]}{[2TP(1-P)]}$	t_i is the number of total individuals in the i^{th} census tract and p_i, is the proportion who are Black individuals; T is the number of total individuals in all census tracts in the PUMA, and P is the proportion of T comprised of Black individuals			
Index of Isolation					
Main analyses[212]	$\sum_{i=1}^{n}\left[\left(\frac{x_i}{X}\right)\left(\frac{x_i}{t_i}\right)\right]$	x_i, t_i are numbers of Black and total (Black and white) individuals in the i^{th} of n census tracts; X is the total number of Black individuals in all n census tracts of one PUMA	Assesses the likelihood that individuals of a given race will encounter only individuals of that same race within a neighborhood; range 0 (not segregated) to 1 (completely segregated)	Tertiles (tertile 3 = greatest segregation)[64]	Table B03002, "Hispanic or Latino Origin by Race", for vintages 2013 and 2018
Sensitivity analyses		As above, except that t_i is total number of individuals in the i^{th} census tract			
Index of Concentration at the Extremes					
Main analyses[216]	$\frac{A_i-P_i}{T_i}$	A_i, P_i, T_i are numbers of most privileged, least privileged, and all individuals in the i^{th} PUMA. Most privileged were defined as non-Hispanic white households earning $100,000+ annually and least privileged as Black households earning <$25,000 annually[218 221 223]	Ranges from -1, indicating that a neighborhood is entirely composed of those with the least privilege, to +1, for neighborhoods entirely composed of those with the most privilege	Quintiles (quintile 5 = greatest concentration of privilege)[219 222]	Table B19001, "Household income in the past 12 months by race/ethnicity", for vintages 2013 and 2018 (income in inflation-adjusted dollars)
Sensitivity analyses		As above, except that most privileged were defined as non-Hispanic white $200,000+; least privileged as Black <$35,000			
Educational Inequity Ratio					
Main analyses[200 201 203]	$\frac{b_i/B_i}{w_i/W_i}$	b_i, w_i, B_i, W_i are numbers of Black and non-Hispanic white individuals aged 25 years or older with a Bachelor's degree or higher, and total numbers of Black and non-Hispanic white individuals aged 25 years or older, in the i^{th} PUMA, respectively	Values between 0 and 1 indicate Black individuals have a proportionately lower educational attainment than white individuals in a neighborhood, while values >1 indicate the reverse. For	Tertiles (reverse-coded so that tertile 3 = greatest inequity)[200]	Table C15002, "Sex by educational attainment for the population 25 years and over", for vintages 2013 and 2018

Use	Formula	Variable definitions	Range and interpretation	Coding	ACS data sources
			regression, values >1 were truncated to 1		

Abbreviations: ACS, American Community Survey; PUMA, Public Use Microdata Area.

Table A15: Structural racism measures and other PUMA-level characteristics stratified by PUMA, with stillbirth rates and numbers, NYC 2009-2018

PUMA	Dissimilarity [a]		Isolation [a]		ICE [b]		Ed Inequity [c]		Poverty [d]		Ed Attainment [e]		Prop NHB [f]		Stillbirths, n	All births, n	SBR
	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	8,177	1,077,041	7.6
Bronx																	
3701	0.60	0.56	0.56	0.54	0.11	0.12	0.50	0.55	0.16	0.19	0.82	0.82	0.13	0.12	70	10,889	6.4
3702	0.61	0.61	0.96	0.96	-0.16	-0.13	0.76	0.70	0.21	0.22	0.80	0.80	0.68	0.65	204	17,493	11.7
3703	0.82	0.78	0.82	0.83	0.03	0.04	0.95	0.94	0.17	0.14	0.82	0.85	0.26	0.28	88	9,698	9.1
3704	0.55	0.53	0.67	0.68	-0.01	0.00	0.89	0.90	0.20	0.20	0.75	0.78	0.21	0.21	81	13,268	6.1
3705	0.70	0.68	0.93	0.94	-0.19	-0.18	0.57	0.58	0.32	0.31	0.61	0.64	0.31	0.31	324	27,381	11.8
3706	0.44	0.36	0.77	0.76	-0.08	-0.06	0.69	0.59	0.30	0.31	0.67	0.70	0.18	0.15	165	21,996	7.5
3707	0.39	0.31	0.95	0.96	-0.16	-0.16	0.54	0.71	0.34	0.37	0.64	0.65	0.27	0.27	169	22,302	7.6
3708	0.41	0.35	0.96	0.94	-0.17	-0.14	0.66	0.47	0.32	0.35	0.62	0.66	0.32	0.29	210	25,126	8.4
3709	0.43	0.36	0.93	0.92	-0.12	-0.10	0.93	0.96	0.25	0.30	0.70	0.72	0.30	0.29	229	24,100	9.5
3710	0.37	0.37	0.93	0.94	-0.18	-0.16	0.49	0.51	0.29	0.32	0.55	0.61	0.27	0.29	250	24,495	10.2
Manhattan																	
3801	0.54	0.51	0.55	0.48	0.02	0.06	0.36	0.40	0.19	0.20	0.69	0.72	0.08	0.08	123	22,833	5.4
3802	0.58	0.45	0.67	0.59	0.00	0.05	0.31	0.35	0.23	0.20	0.79	0.81	0.22	0.22	70	11,255	6.2
3803	0.34	0.30	0.85	0.81	-0.22	-0.14	0.33	0.34	0.22	0.21	0.81	0.82	0.60	0.55	144	15,646	9.2
3804	0.45	0.45	0.77	0.78	-0.11	-0.09	0.32	0.31	0.22	0.24	0.72	0.74	0.30	0.31	111	15,240	7.3
3805	0.51	0.55	0.13	0.11	0.43	0.46	0.53	0.49	0.07	0.06	0.97	0.98	0.03	0.02	93	24,988	3.7
3806	0.46	0.48	0.22	0.19	0.38	0.43	0.31	0.40	0.10	0.09	0.94	0.95	0.07	0.05	98	24,486	4.0
3807	0.36	0.28	0.14	0.14	0.33	0.36	0.48	0.47	0.11	0.12	0.94	0.94	0.06	0.05	69	14,745	4.7
3808	0.33	0.42	0.08	0.11	0.39	0.43	0.59	0.66	0.10	0.09	0.97	0.97	0.03	0.03	58	12,192	4.8
3809	0.53	0.54	0.43	0.47	0.12	0.13	0.27	0.32	0.21	0.22	0.72	0.74	0.07	0.08	77	14,989	5.1
3810	0.30	0.28	0.05	0.05	0.44	0.50	0.78	0.67	0.09	0.08	0.95	0.96	0.02	0.02	50	17,940	2.8
Staten Island																	
3901	0.65	0.60	0.07	0.05	0.37	0.40	0.91	0.70	0.10	0.22	0.91	0.93	0.01	0.01	59	14,606	4.0
3902	0.41	0.50	0.13	0.15	0.26	0.30	0.71	0.64	0.15	0.12	0.89	0.88	0.03	0.04	85	13,815	6.2
3903	0.59	0.60	0.63	0.63	0.09	0.09	0.71	0.67	0.21	0.12	0.84	0.84	0.23	0.21	200	23,133	8.7
Brooklyn																	
4001	0.56	0.42	0.26	0.19	0.16	0.25	0.38	0.39	0.22	0.15	0.81	0.84	0.03	0.04	223	34,812	6.4
4002	0.59	0.42	0.77	0.62	-0.07	0.00	0.20	0.28	0.28	0.25	0.58	0.73	0.18	0.18	117	15,121	7.7
4003	0.65	0.48	0.90	0.78	-0.22	-0.10	0.47	0.42	0.27	0.22	0.76	0.82	0.58	0.49	258	22,902	11.3
4004	0.53	0.47	0.59	0.55	0.16	0.24	0.36	0.40	0.13	0.12	0.88	0.90	0.27	0.25	89	15,672	5.7
4005	0.48	0.52	0.41	0.47	0.35	0.43	0.39	0.40	0.09	0.10	0.91	0.93	0.07	0.07	91	16,899	5.4
4006	0.54	0.47	0.85	0.79	-0.18	-0.09	0.25	0.31	0.25	0.21	0.81	0.84	0.64	0.58	137	12,975	10.6
4007	0.40	0.48	0.98	0.97	-0.36	-0.34	0.59	0.34	0.32	0.30	0.73	0.77	0.76	0.72	203	13,432	15.1
4008	0.61	0.48	0.93	0.94	-0.22	-0.20	0.63	0.74	0.34	0.29	0.75	0.80	0.52	0.52	298	26,685	11.2
4009	0.74	0.74	0.89	0.90	-0.01	0.00	0.73	0.77	0.14	0.14	0.87	0.88	0.62	0.62	241	22,561	10.7
4010	0.40	0.40	0.98	0.97	-0.24	-0.20	0.54	0.53	0.22	0.17	0.84	0.86	0.90	0.87	272	19,610	13.9

PUMA	Dissimilarity [a]		Isolation [a]		ICE [b]		Ed Inequity [c]		Poverty [d]		Ed Attainment [e]		Prop NHB [f]		Stillbirths, n	All births, n	SBR
	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	2013 [g]	2018 [g]	8,177	1,077,041	7.6
4011	0.45	0.40	0.86	0.79	-0.21	-0.11	0.33	0.33	0.25	0.21	0.82	0.86	0.70	0.64	143	15,126	9.5
4012	0.39	0.47	0.25	0.26	0.09	0.13	0.48	0.43	0.30	0.24	0.59	0.62	0.03	0.03	151	26,719	5.7
4013	0.48	0.45	0.05	0.15	0.18	0.23	0.83	0.96	0.20	0.18	0.80	0.82	0.01	0.02	108	17,554	6.2
4014	0.71	0.56	0.14	0.09	0.12	0.17	1.00	1.00	0.32	0.26	0.76	0.77	0.02	0.02	329	52,375	6.3
4015	0.75	0.71	0.80	0.74	0.00	0.06	0.45	0.43	0.26	0.20	0.83	0.83	0.34	0.31	231	25,496	9.1
4016	0.62	0.58	0.38	0.33	0.18	0.21	0.42	0.65	0.20	0.17	0.86	0.85	0.03	0.04	116	20,978	5.5
4017	0.47	0.44	0.05	0.05	0.11	0.12	1.00	1.00	0.22	0.23	0.71	0.74	0.01	0.01	103	24,698	4.2
4018	0.82	0.81	0.64	0.63	0.05	0.07	0.29	0.40	0.24	0.25	0.81	0.82	0.12	0.11	77	11,805	6.5
Queens																	
4101	0.71	0.67	0.61	0.59	0.10	0.17	0.40	0.48	0.20	0.17	0.82	0.86	0.07	0.07	102	19,353	5.3
4102	0.74	0.70	0.73	0.68	0.02	0.04	0.47	0.41	0.26	0.22	0.70	0.71	0.05	0.05	132	25,524	5.2
4103	0.63	0.68	0.30	0.39	0.11	0.10	0.76	0.57	0.23	0.23	0.80	0.77	0.02	0.02	145	27,041	5.4
4104	0.54	0.52	0.17	0.19	0.19	0.20	1.00	0.93	0.14	0.12	0.89	0.88	0.02	0.02	27	6,503	4.2
4105	0.80	0.81	0.94	0.94	0.00	0.00	0.87	0.85	0.12	0.11	0.87	0.88	0.56	0.56	151	16,154	9.4
4106	0.53	0.50	0.48	0.49	0.07	0.08	0.72	0.68	0.21	0.19	0.85	0.86	0.12	0.12	97	17,341	5.6
4107	0.53	0.58	0.65	0.70	-0.01	0.00	0.70	0.93	0.28	0.23	0.67	0.73	0.07	0.06	132	25,894	5.1
4108	0.40	0.31	0.10	0.10	0.18	0.18	0.85	0.99	0.14	0.14	0.92	0.92	0.03	0.03	47	12,954	3.6
4109	0.39	0.33	0.18	0.11	0.11	0.16	0.42	0.74	0.21	0.15	0.80	0.82	0.01	0.01	62	15,712	4.0
4110	0.48	0.47	0.09	0.07	0.16	0.22	0.87	0.98	0.20	0.16	0.80	0.85	0.01	0.01	110	19,234	5.7
4111	0.44	0.49	0.45	0.44	0.06	0.07	0.77	0.65	0.20	0.20	0.77	0.78	0.07	0.06	134	18,472	7.3
4112	0.60	0.53	0.98	0.98	-0.14	-0.12	1.00	1.00	0.23	0.17	0.79	0.81	0.64	0.62	301	28,979	10.4
4113	0.77	0.77	0.79	0.79	0.06	0.09	0.72	0.72	0.18	0.17	0.78	0.77	0.16	0.14	98	12,709	7.7
4114	0.64	0.64	0.75	0.76	0.00	0.04	0.5	0.46	0.22	0.17	0.78	0.80	0.37	0.36	107	12,801	8.4

Abbreviations: ICE, Index of Concentration at the Extremes; NHB, non-Hispanic Black; PUMA, Public Use Microdata Area; SBR, stillbirth rate (number of stillbirths per 1000 total births).

[a] *Indices of Dissimilarity and Isolation range from 0, less segregated, to 1, most segregated.*

[b] *ICE ranges from -1, population concentration of least privileged, to +1, population concentration of most privileged.*

[c] *Educational inequity ranges from 0, Black proportion of college graduates is lower than white proportion, to 1, complete equity; values greater than 1 (indicating Black proportion of college graduates is higher than white proportion) were truncated to 1, and tertiles were reverse-coded so that tertile 1 represents least inequity and tertile 3 represents greatest inequity.*

[d] *"Poverty" is percent of the PUMA population under the poverty threshold as set by the NYC Office of the Mayor's Center for Economic Opportunity using 5-year averages.*

[e] *"Ed attainment" is proportion of the PUMA population 25 or older with at least a high school diploma.*

[f] *"Prop NHB" is percent of the PUMA population consisting of non-Hispanic Black residents.*

[g] *2013 data are averages over 2009-2013. 2018 data are averages over 2014-2018.*

Table A16: Structural racism measures and other PUMA-level characteristics: Ranges for each level of categorical versions of covariates, NYC 2009-2018

	2013 vintage [g]	2018 vintage [g]
ICE [b]		
Quintile 1	-0.36, -0.16	-0.34, -0.11
Quintile 2	-0.16, 0.00	-0.10, 0.04
Quintile 3	0.00, 0.09	0.04, 0.10
Quintile 4	0.10, 0.18	0.12, 0.22
Quintile 5	0.18, 0.44	0.23, 0.50
Isolation [a]		
Tertile 1	0.05, 0.41	0.05, 0.44
Tertile 2	0.43, 0.79	0.47, 0.78
Tertile 3	0.80, 0.98	0.79, 0.98
Dissimilarity [a]		
Tertile 1	0.30, 0.46	0.28, 0.45
Tertile 2	0.47, 0.60	0.47, 0.55
Tertile 3	0.60, 0.82	0.56, 0.81
Educational Inequity [c]		
Tertile 1	0.72, 1.00	0.70, 1.00
Tertile 2	0.48, 0.72	0.47, 0.70
Tertile 3	0.20, 0.47	0.28, 0.46
PUMA % poverty [d]		
<median	0.07, 0.21	0.06, 0.20
median+	0.21, 0.34	0.20, 0.37
PUMA % Black [f]		
<median	0.01, 0.13	0.01, 0.12
median+	0.16, 0.90	0.14, 0.87
PUMA % HS [e]		
<median	0.55, 0.80	0.61, 0.82
median+	0.80, 0.97	0.82, 0.98

Abbreviations: HS, high school; ICE, Index of Concentration at the Extremes; PUMA, Public Use Microdata Area.
[a] Indices of Dissimilarity and Isolation range from 0, less segregated, to 1, most segregated. Tertile 1 indicates low isolation or dissimilarity; tertile 3 indicates high isolation or dissimilarity.
[b] ICE ranges from -1, population concentration of least privileged, to +1, population concentration of most privileged. Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[c] Educational inequity ranges from 0, Black proportion of college graduates is lower than white proportion, to 1, complete equity; values greater than 1 (indicating Black proportion of college graduates is higher than white proportion) were truncated to 1, and tertiles were reverse-coded so that tertile 1 represents least inequity and tertile 3 represents greatest inequity.
[d] PUMA % poverty is percent of the PUMA population under the poverty threshold as set by the NYC Office of the Mayor's Center for Economic Opportunity using 5-year averages.
[e] PUMA % HS is proportion of the PUMA population 25 or older with at least a high school diploma.
[f] PUMA % Black is percent of the PUMA population consisting of non-Hispanic Black residents.
[g] 2013 data are averages over 2009-2013. 2018 data are averages over 2014-2018.

Table A17: Stillbirths and livebirths stratified by selected PUMA-level covariates and race, NYC 2009-2018

Black births	**<Median PUMA % Black (n=22210)**		**Median+ PUMA % Black (n=199715)**	
	Stillbirths, n	**Livebirths, n**	**Stillbirths, n**	**Livebirths, n**
<Median PUMA % poverty (n=75644)	209	14711	788	59936
Median+ PUMA % poverty (n=146281)	108	7182	1841	137150
White births	**<Median PUMA % Black (n=253332)**		**Median+ PUMA % Black (n=71726)**	
	Stillbirths, n	**Livebirths, n**	**Stillbirths, n**	**Livebirths, n**
<Median PUMA % poverty (n=196790)	638	168196	130	27826
Median+ PUMA % poverty (n=128268)	426	84072	267	43503

Abbreviations: PUMA, Public Use Microdata Area.

Table A18: Comparison of births with and without PUMA (Public Use Microdata Area) data, NYC (2009-2018)

	Livebirths, n (column %)		Stillbirths, n (column %)	
	PUMA	No PUMA	PUMA	No PUMA
n	1,068,848	16	7,859	318
Birth characteristics				
Sex				
Female	521,086 (49%)	4 (25%)	3,003 (38%)	116 (36%)
Male	547,762 (51%)	12 (75%)	3,545 (45%)	139 (44%)
Missing	0 (0%)	0 (0%)	1,311 (17%)	63 (20%)
Gestational age, completed weeks				
20-27	5,323 (0%)	0 (0%)	4,747 (60%)	236 (74%)
28-36	71,726 (7%)	2 (13%)	1,898 (24%)	56 (18%)
37-47	991,799 (93%)	14 (88%)	1,214 (15%)	26 (8%)
Year of birth				
2009	112,508 (11%)	3 (19%)	895 (11%)	44 (14%)
2010	110,609 (10%)	0 (0%)	856 (11%)	41 (13%)
2011	109,319 (10%)	2 (13%)	821 (10%)	90 (28%)
2012	109,403 (10%)	0 (0%)	760 (10%)	70 (22%)
2013	106,509 (10%)	0 (0%)	751 (10%)	23 (7%)
2014	107,545 (10%)	0 (0%)	806 (10%)	38 (12%)
2015	106,954 (10%)	0 (0%)	746 (9%)	9 (3%)
2016	105,181 (10%)	5 (31%)	755 (10%)	3 (1%)
2017	101,833 (10%)	1 (6%)	731 (9%)	0 (0%)
2018	98,987 (9%)	5 (31%)	738 (9%)	0 (0%)
Maternal characteristics				
Maternal age, years				
10-19	48,297 (5%)	0 (0%)	444 (6%)	25 (8%)
20-34	778,417 (73%)	13 (81%)	5,300 (67%)	215 (68%)
35-63	242,134 (23%)	3 (19%)	2,110 (27%)	78 (25%)
Missing	0 (0%)	0 (0%)	5 (0%)	0 (0%)
Borough of maternal residence				
Bronx	194,067 (18%)	3 (19%)	1,781 (23%)	89 (28%)
Brooklyn	392,238 (37%)	3 (19%)	3,194 (41%)	76 (24%)
Manhattan	174,303 (16%)	4 (25%)	906 (12%)	60 (19%)
Queens	257,029 (24%)	2 (13%)	1,634 (21%)	82 (26%)
Staten Island	51,211 (5%)	4 (25%)	344 (4%)	11 (3%)
Maternal education				
High school or less	477,108 (45%)	7 (44%)	2,431 (31%)	105 (33%)
Any college	434,888 (41%)	8 (50%)	1,194 (15%)	45 (14%)
More than college	153,382 (14%)	0 (0%)	268 (3%)	10 (3%)
Missing	3,470 (0%)	1 (6%)	3,966 (50%)	158 (50%)
Maternal race/ethnicity				
Non-Hispanic Black	218,979 (20%)	5 (31%)	2,946 (37%)	117 (37%)
Non-Hispanic white	323,597 (30%)	4 (25%)	1,461 (19%)	51 (16%)
Hispanic	333,964 (31%)	5 (31%)	2,004 (25%)	87 (27%)
Non-Hispanic Asian	175,619 (16%)	1 (6%)	762 (10%)	21 7%)
Non-Hispanic Native American	513 (0%)	0 (0%)	4 (0%)	0 (0%)
Other	13,189 (1%)	1 (6%)	54 (1%)	2 (1%)
Missing	2,987 (0%)	0 (0%)	628 (8%)	40 (13%)
Medical risk factors				
Yes	537,354 (50%)	8 (50%)	3,605 (46%)	125 (39%)
No	531,494 (50%)	8 (50%)	4,217 (54%)	192 (60%)
Missing	0 (0%)	0 (0%)	37 (0%)	1 (0%)
Prenatal care (PNC) visits				
<median	482,784 (45%)	10 (63%)	6,145 (78%)	266 (84%)
median+	586,064 (55%)	6 (38%)	1,714 (22%)	52 (16%)

Table A19: Pearson correlation coefficients for correlation [e] between PUMA-level characteristics, 2013 and 2018

	Isolation	Dissimilarity	ICE	Ed Inequity	PUMA % Black [c]	PUMA % HS [b]
2013 [d]						
Dissimilarity	0.28					
ICE	-0.86	-0.09				
Ed Inequity	-0.19	0.09	0.11			
PUMA % Black [c]	0.79	0.07	-0.77	-0.10		
PUMA % HS [b]	-0.47	0.00	0.64	0.12	-0.11	
PUMA Poverty [a]	0.53	0.06	-0.77	-0.10	0.31	-0.83
2018 [d]						
Dissimilarity	0.23					
ICE	-0.86	-0.02				
Ed Inequity	-0.19	0.08	0.08			
PUMA % Black [c]	0.79	0.04	-0.74	-0.16		
PUMA % HS [b]	-0.46	0.03	0.65	0.07	-0.07	
PUMA Poverty [a]	0.52	-0.13	-0.72	-0.09	0.23	-0.84

Abbreviations: ICE, Index of Concentration at the Extremes; NH, non-Hispanic; PUMA, Public Use Microdata Area.

[a] PUMA Poverty is percent of the PUMA population under the poverty threshold as set by the NYC Office of the Mayor's Center for Economic Opportunity using 5-year averages.

[b] PUMA % HS is proportion of the PUMA population 25 or older with at least a high school diploma.

[c] PUMA % Black is percent of the PUMA population consisting of non-Hispanic Black residents.

[d] 2013: correlation of 2013 data (which were averages over 2009-2013); 2018: correlation of 2018 data (which were averages over 2014-2018).

[e] Correlations were calculated at the PUMA rather than individual level.

Table A20: Odds ratios for associations between four structural racism measures and stillbirth, comparing models with and without terms for interaction between structural racism and race, in 546,983 non-Hispanic Black and white births, NYC (2009-2018)

	No interaction, OR (95% CI) [a]	Interaction [e], OR (95% CI) [a]	*P* value [f]
Dissimilarity			
Continuous [d]			
Dissimilarity	1.06 (1.00, 1.12)	1.04 (0.96, 1.13)	
white	ref	ref	
Black	1.94 (1.76, 2.15)	1.93 (1.74, 2.15)	
Black*Dissimilarity		1.02 (0.93, 1.12)	<0.64
Categorical [b]			
Tertile 1	ref	ref	
Tertile 2	1.09 (0.97, 1.23)	0.98 (0.83, 1.15)	
Tertile 3	1.16 (1.03, 1.31)	1.07 (0.89, 1.29)	
white	ref	ref	
Black	1.95 (1.76, 2.16)	1.72 (1.44, 2.04)	
Black*Tertile 2		1.24 (1.00, 1.53)	<0.05
Black*Tertile 3		1.15 (0.93, 1.44)	<0.20
Isolation			
Continuous [d]			
Isolation	0.98 (0.87, 1.11)	1.04 (0.92, 1.18)	
white	ref	ref	
Black	1.96 (1.76, 2.18)	2.07 (1.86, 2.30)	
Black*Isolation		0.77 (0.69, 0.86)	<0.01
Categorical [b]			
Tertile 1	ref	ref	
Tertile 2	0.90 (0.75, 1.08)	1.00 (0.82, 1.23)	
Tertile 3	0.93 (0.70, 1.23)	1.16 (0.86, 1.58)	
white	ref	ref	
Black	1.98 (1.78, 2.20)	3.14 (2.58, 3.83)	
Black*Tertile 2		0.58 (0.45, 0.75)	<0.01
Black*Tertile 3		0.51 (0.39, 0.65)	<0.01
Educational Inequity			
Continuous [d]			
Educational Inequity	1.04 (0.98, 1.10)	1.00 (0.92, 1.08)	
white	ref	ref	
Black	1.95 (1.76, 2.17)	1.98 (1.78, 2.19)	
Black* Ed Inequity		1.07 (0.98, 1.18)	<0.15
Categorical [b]			
Tertile 1	ref	ref	
Tertile 2	0.92 (0.81, 1.04)	1.05 (0.86, 1.27)	
Tertile 3	0.90 (0.78, 1.03)	1.01 (0.83, 1.22)	
white	ref	ref	
Black	1.95 (1.76, 2.16)	2.27 (1.89, 2.73)	
Black*Tertile 2		0.80 (0.63, 1.01)	<0.06
Black*Tertile 3		0.82 (0.66, 1.03)	<0.08
ICE			
Continuous [d]			
ICE	1.10 (0.93, 1.30)	1.05 (0.89, 1.24)	
white	ref	ref	
Black	1.97 (1.78, 2.19)	2.01 (1.81, 2.22)	
Black*ICE		1.23 (1.11, 1.36)	<0.01
Categorical [c]			
Quintile 1	ref	ref	
Quintile 2	1.11 (0.95, 1.29)	0.90 (0.66, 1.22)	
Quintile 3	1.27 (0.99, 1.64)	0.98 (0.70, 1.39)	

	No interaction, OR (95% CI) [a]	Interaction [e], OR (95% CI) [a]	*P* value [f]
Quintile 4	1.37 (1.01, 1.85)	0.97 (0.67, 1.39)	
Quintile 5	1.44 (1.01, 2.06)	1.03 (0.69, 1.55)	
white	ref	ref	
Black	1.99 (1.79, 2.21)	1.45 (1.16, 1.81)	
Black*Quintile 2		1.26 (0.93, 1.71)	<0.14
Black*Quintile 3		1.31 (0.97, 1.76)	<0.08
Black*Quintile 4		1.80 (1.29, 2.49)	<0.01
Black*Quintile 5		1.90 (1.36, 2.64)	<0.01

Abbreviations: CI, confidence interval; ICE, Index of Concentration at the Extremes; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age, education, and race, proportion of the PUMA population under the poverty line, and proportion of PUMA residents who are non-Hispanic Black.
[b] Tertile 1 indicates low isolation, dissimilarity, or educational inequity; tertile 3 indicates high isolation; dissimilarity, or educational inequity.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[d] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.
[e] Interaction models included terms for interaction between the structural racism measure and race (NH Black, NH white).
[f] P values for cross-product terms from the Wald test.

Table A21: Odds ratios (95% CI) for associations between two structural racism measures (Isolation and ICE) and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018): Continuous versions of exposures

	NH Black (n=221,925) [a]	NH white (n=325,058) [a]
Isolation [b]	0.80 (0.67, 0.95)	1.05 (0.88, 1.25)
PUMA % poverty	1.06 (0.97, 1.16)	1.06 (0.96, 1.18)
PUMA % Black	1.07 (0.94, 1.21)	1.03 (0.86, 1.23)
ICE [b]	1.31 (1.03, 1.65)	1.08 (0.85, 1.36)
PUMA % poverty	1.14 (0.99, 1.31)	1.11 (0.95, 1.30)
PUMA % Black	1.10 (0.95, 1.29)	1.12 (0.93, 1.35)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; PUMA, Public Use Microdata Area; ref, reference level.
[a] Adjusted for year, maternal age, proportion of the PUMA population under the poverty line ("PUMA % poverty"), proportion of PUMA residents who are non-Hispanic Black ("PUMA % Black"), and maternal education.
[b] ORs represent change in odds of stillbirth with a 1 standard deviation increase in the exposure or covariate.

Table A22: Summary of results of sensitivity analyses

Sensitivity analysis	Evidence of interaction beyond ICE and Isolation?	Main results – non-Hispanic Black births	Main results – non-Hispanic white births
1. Model specifications	No	Increasing isolation was associated with reduced odds of stillbirth in all model specifications (Table A23). ICE quintiles 4 and 5 vs 1 were associated with increased odds of stillbirth in all model specifications.	Increasing isolation was associated with increased odds of stillbirth in the model that adjusted only for individual-level covariates; otherwise there was no evidence of an association. ICE was not associated with stillbirth in any model.
2. Extreme versions of exposures	No	Residing in a PUMA in the 25th centile for ICE values (concentration of privilege) was associated with 36% greater odds of stillbirth (95% CI 1.01, 1.82) (Table A24). Residing in a PUMA in the 25th centile for Isolation values (greater vs less isolation) was not associated with stillbirth.	There was no association between extreme ICE or Isolation values and stillbirth.
3. Alternative formulas for exposures	Dissimilarity (Table A25)	Associations between Isolation and stillbirth were no longer protective (Table A26). ICE quintiles 4 and 5 remained associated with stillbirth. Dissimilarity tertile 2 vs 1 was associated with increased odds of stillbirth.	Associations between Isolation and stillbirth and ICE and stillbirth remained non-significant. There was no evidence of associations between Dissimilarity and stillbirth.
4. Different definitions of the population	No	In populations excluding births in PUMAs with fewer than 5 and fewer than 10 stillbirths, ICE quintiles 4 vs 1 and 5 vs 1 remained associated with increased odds of stillbirth, and increased Isolation remained associated with reduced odds of stillbirth (Table A27).	Associations between ICE and stillbirth and between Isolation and stillbirth remained non-significant.
5. Data sources	Educational Inequity (Table A28)	ICE quintiles 4 and 5 remained associated with increased odds of stillbirth and increased Isolation remained protective (Table A29). Greater educational inequity was associated with 24% lower odds of stillbirth in vintage 2013 births (95% CI 0.59, 0.98).	ICE quintile 5 vs 1 was associated with increased odds of stillbirth in vintage 2013 births (OR 4.11, 95% CI 1.02, 16.58). There was no evidence of associations between Isolation or Educational Inequity and stillbirth.
6. Sibling clusters	No	Larger ICE quintiles were associated with increased odds of stillbirth in 2009, 2016, and 2018, but not 2011 (Table A30). Increased Isolation was associated with reduced odds of stillbirth only in 2011.	Increased ICE was associated with increased odds of stillbirth in 2011 only. There was no evidence of associations between Isolation and stillbirth.

Abbreviations: CI, confidence interval; ICE, Index of Concentration at the Extremes; NH, non-Hispanic; OR, odds ratio; PUMA, Public Use Microdata Area.

Table A23: Sensitivity analysis 1: Different model specifications: Odds ratios (95% CIs) for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

Change from main model:	**Unadjusted**		**Main model [d]**		**PUMA-level covariates removed**		**Maternal education removed**		**Additional adjustment for PUMA % HS**	
Adjusted for:	-		Year of birth, maternal age, PUMA % poverty, PUMA % NHB, maternal education		Year of birth, maternal age, maternal education		Year of birth, maternal age, PUMA % poverty, PUMA % NHB		Year of birth, maternal age, PUMA % poverty, PUMA % NHB, maternal education, PUMA % HS	
	NH Black, n=221,925	NH white, n=325,057	NH Black, n=221,925	NH white, n=325,057	NH Black, n=221,925	NH white, n=325,057	NH Black, n=221,925	NH white, n=325,057	NH Black, n=221,925	NH white, n=325,057
Isolation										
Continuous [c]	0.93 (0.86, 1.00)	1.22 (1.10, 1.35)	0.80 (0.67, 0.95)	1.05 (0.88, 1.25)	0.88 (0.79, 0.97)	1.10 (1.00, 1.21)	0.79 (0.69, 0.89)	1.02 (0.87, 1.21)	0.77 (0.63, 0.95)	1.09 (0.90, 1.31)
Categorical										
Tertile 1 [a]	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
Tertile 2	0.67 (0.56, 0.81)	1.00 (0.80, 1.24)	0.61 (0.47, 0.80)	1.04 (0.81, 1.35)	0.64 (0.51, 0.81)	1.05 (0.86, 1.30)	0.61 (0.50, 0.74)	0.89 (0.71, 1.12)	0.61 (0.46, 0.80)	1.08 (0.83, 1.40)
Tertile 3 [a]	0.74 (0.62, 0.88)	1.60 (1.26, 2.05)	0.60 (0.42, 0.86)	1.28 (0.77, 2.14)	0.67 (0.54, 0.83)	1.28 (1.01, 1.61)	0.57 (0.43, 0.70)	1.21 (0.78, 1.90)	0.59 (0.41, 0.87)	1.32 (0.79, 2.21)
ICE										
Continuous [c]	1.02 (0.96, 1.10)	0.78 (0.71, 0.85)	1.31 (1.03, 1.65)	1.08 (0.85, 1.36)	1.09 (1.00, 1.19)	0.92 (0.83, 1.01)	1.21 (0.99, 1.47)	0.85 (0.69, 1.05)	1.40 (1.02, 1.92)	1.01 (0.74, 1.38)
Categorical										
Quintile 1 [b]	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
Quintile 2	0.87 (0.78, 0.98)	0.79 (0.58, 1.06)	1.12 (0.95, 1.33)	0.99 (0.68, 1.45)	1.03 (0.89, 1.19)	0.85 (0.61, 1.19)	0.95 (0.83, 1.09)	0.91 (0.65, 1.27)	1.15 (0.96, 1.36)	0.98 (0.67, 1.44)
Quintile 3	0.93 (0.79, 1.08)	0.61 (0.45, 0.84)	1.27 (0.95, 1.70)	1.10 (0.66, 1.85)	1.06 (0.86, 1.30)	0.83 (0.59, 1.16)	1.16 (0.92, 1.45)	0.73 (0.46, 1.15)	1.35 (0.98, 1.87)	1.07 (0.63, 1.82)
Quintile 4	1.10 (0.89, 1.35)	0.55 (0.41, 0.73)	1.70 (1.16, 2.49)	1.13 (0.62, 2.05)	1.34 (1.03, 1.75)	0.78 (0.58, 1.06)	1.46 (1.08, 1.97)	0.68 (0.40, 1.16)	1.85 (1.20, 2.87)	1.07 (0.56, 2.03)
Quintile 5 [b]	1.23 (1.00, 1.52)	0.51 (0.38, 0.68)	1.90 (1.20, 2.99)	1.27 (0.65, 2.49)	1.36 (1.04, 1.78)	0.78 (0.58, 1.06)	1.76 (1.23, 2.52)	0.75 (0.41, 1.37)	2.15 (1.24, 3.70)	1.18 (0.56, 2.47)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.

[a] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.

[b] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

[c] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.

[d] Main model from Table 5 repeated here for convenience.

Table A24: Sensitivity analysis 2: Extreme versions of exposures: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	**OR (95% CI) [a]**
	NH Black (n=221,925)	NH white (n=325,057)
Index of Isolation		
<75th centile	ref	ref
75th centile	1.07 (0.89, 1.28)	1.12 (0.82, 1.54)
Index of Concentration at the Extremes		
<75th centile	ref	ref
75th centile	1.36 (1.01, 1.82)	1.08 (0.84, 1.38)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a] Adjusted for year, maternal age, education, proportion of the PUMA population under the poverty line, and proportion of PUMA residents who are non-Hispanic Black.

Table A25: Sensitivity analysis 3: Interaction assessment for alternative [e] versions of exposures: Odds ratios for associations between three structural racism measures and stillbirth, comparing models with and without terms for interaction between structural racism and race, in 546,983 non-Hispanic Black and white births, NYC (2009-2018)

	No interaction, OR (95% CI) [a]	Interaction, OR (95% CI) [a,e]	*P* value [f]
Index of Dissimilarity [e]			
Continuous [d]			<0.03
Dissimilarity	1.05 (0.99, 1.12)	0.98 (0.89, 1.07)	
white	ref	ref	
Black	1.96 (1.77, 2.17)	1.92 (1.74, 2.13)	
Black*Dissimilarity		1.12 (1.01, 1.23)	<0.03
Categorical			<0.01
Tertile 1 [b]	ref	ref	
Tertile 2	1.12 (0.97, 1.30)	0.87 (0.71, 1.07)	
Tertile 3 [b]	1.10 (0.95, 1.28)	0.89 (0.72, 1.09)	
white	ref	ref	
Black	1.96 (1.77, 2.18)	1.50 (1.24, 1.80)	
Black*Tertile 2		1.51 (1.20, 1.90)	<0.01
Black*Tertile 3 [b]		1.37 (1.08, 1.74)	<0.01
Index of Isolation [e]			
Continuous [d]			<0.01
Isolation	1.16 (0.94, 1.43)	1.19 (0.96, 1.48)	
white	ref	ref	
Black	1.94 (1.75, 2.15)	2.01 (1.81, 2.23)	
Black*Isolation		0.88 (0.80, 0.97)	<0.01
Categorical			<0.01
Tertile 1 [b]	ref	ref	
Tertile 2	1.03 (0.86, 1.23)	1.14 (0.93, 1.40)	
Tertile 3 [b]	1.05 (0.82, 1.33)	1.18 (0.91, 1.52)	
white	ref	ref	
Black	1.95 (1.75, 2.16)	2.83 (2.30, 3.49)	
Black*Tertile 2		0.63 (0.48, 0.83)	<0.01
Black*Tertile 3 [b]		0.61 (0.48, 0.79)	<0.01
Index of Concentration at the Extremes [e]			
Continuous [d]			<0.01
ICE	1.03 (0.86, 1.24)	0.97 (0.81, 1.17)	
white	ref	ref	
Black	1.96 (1.76, 2.17)	2.00 (1.81, 2.22)	
Black*ICE		1.20 (1.09, 1.33)	<0.01
Categorical			<0.01
Quintile 1 [c]	ref	ref	
Quintile 2	1.15 (0.94, 1.40)	1.31 (0.95, 1.79)	
Quintile 3	1.21 (0.90, 1.63)	1.03 (0.71, 1.50)	
Quintile 4	1.27 (0.90, 1.79)	1.04 (0.71, 1.52)	
Quintile 5 [c]	1.40 (0.94, 2.10)	1.17 (0.76, 1.81)	
white	ref	ref	
Black	1.97 (1.77, 2.19)	1.66 (1.35, 2.03)	
Black*Quintile 2		0.86 (0.65, 1.15)	<0.31
Black*Quintile 3		1.24 (0.92, 1.68)	<0.15
Black*Quintile 4		1.66 (1.20, 2.29)	<0.01
Black*Quintile 5 [c]		1.78 (1.28, 2.47)	<0.01

Abbreviations: CI, confidence interval; ICE, Index of Concentration at the Extremes; NH, non-Hispanic; OR, odds ratio; ref, reference level.

[a] Adjusted for year, maternal age, education, and race, proportion of the PUMA population under the poverty line, and proportion of PUMA residents who are non-Hispanic Black.

[b] *Tertile 1 indicates low isolation, tertile 3 indicates high isolation.*
[c] *Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.*
[d] *ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.*
[e] *Interaction models included terms for interaction between the structural racism measure and race (NH Black, NH white).*
[f] *P values for cross-product terms from the Wald test.*
[e] *For definitions of alternative versions of exposures, see Table A14.*

Table A26: Sensitivity analysis 3: For alternative [e] versions of exposures showing evidence of interaction with race: Odds ratios for associations between three structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	NH white (n=325,057)
Index of Isolation [e]		
Continuous [d]	1.42 (0.45, 4.51)	1.28 (0.36, 4.59)
Categorical		
Tertile 1 [b]	ref	ref
Tertile 2	0.78 (0.59, 1.02)	1.14 (0.90, 1.45)
Tertile 3 [b]	0.80 (0.57, 1.11)	1.07 (0.72, 1.59)
Index of Concentration at the Extremes [e]		
Continuous [d]	2.04 (0.39, 10.57)	0.92 (0.17, 5.04)
Categorical		
Quintile 1 [c]	ref	ref
Quintile 2	1.16 (0.93, 1.44)	1.29 (0.84, 1.98)
Quintile 3	1.35 (0.96, 1.90)	0.88 (0.48, 1.65)
Quintile 4	1.79 (1.17, 2.73)	0.91 (0.46, 1.82)
Quintile 5 [c]	2.20 (1.30, 3.72)	1.04 (0.48, 2.28)
Index of Dissimilarity [e]		
Continuous [d]	1.58 (0.90, 2.76)	1.07 (0.54, 2.13)
Categorical		
Tertile 1 [b]	ref	ref
Tertile 2	1.24 (1.01, 1.52)	0.90 (0.72, 1.12)
Tertile 3 [b]	1.17 (0.94, 1.45)	0.96 (0.76, 1.20)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level poverty and proportion of residents who are non-Hispanic Black.
[b] Tertile 1 indicates low structural racism, tertile 3 indicates high structural racism.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 high concentration of privilege.
[d] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.
[e] For definitions of alternative versions of exposures, see Table A14.

Table A27: Sensitivity analysis 4: Excluding PUMAs with fewer than 5 and fewer than 10 stillbirths and stillbirths with reported birthweight <150 grams: Odds ratios for associations between two structural racism measures and stillbirth in restricted populations of non-Hispanic Black and white births, NYC (2009-2018)

	A: Excluding PUMAs with fewer than 5 stillbirths and stillbirths <150 g, OR (95% CI) [a]		B: Excluding PUMAs with fewer than 10 stillbirths and stillbirths <150 g, OR (95% CI) [a]	
	NH Black	**NH white**	**NH Black**	**NH white**
n	219,694 [e]	318,801 [f]	214,496 [g]	307,161 [h]
Index of Isolation				
Continuous [d]	0.75 (0.61, 0.91)	1.03 (0.85, 1.26)	0.73 (0.59, 0.90)	1.06 (0.85, 1.33)
Categorical				
Tertile 1 [b]	ref	ref	ref	ref
Tertile 2	0.55 (0.41, 0.73)	1.02 (0.76, 1.35)	0.53 (0.39, 0.72)	1.04 (0.77, 1.42)
Tertile 3 [b]	0.54 (0.37, 0.79)	1.51 (0.80, 2.84)	0.53 (0.36, 0.79)	1.47 (0.74, 2.93)
Index of Concentration at the Extremes				
Continuous [d]	1.35 (1.05, 1.75)	1.01 (0.79, 1.30)	1.39 (1.06, 1.82)	0.99 (0.76, 1.28)
Categorical				
Quintile 1 [c]	ref	ref	ref	ref
Quintile 2	1.12 (0.94, 1.33)	0.94 (0.62, 1.43)	1.11 (0.93, 1.33)	1.14 (0.70, 1.84)
Quintile 3	1.29 (0.95, 1.75)	0.95 (0.53, 1.70)	1.28 (0.93, 1.75)	1.07 (0.53, 2.18)
Quintile 4	1.83 (1.21, 2.77)	0.93 (0.47, 1.83)	1.95 (1.26, 3.02)	1.02 (0.44, 2.35)
Quintile 5 [c]	1.87 (1.14, 3.04)	1.09 (0.51, 2.33)	1.90 (1.15, 3.15)	1.21 (0.49, 2.98)

Abbreviations: CI, confidence interval; g, grams; NH, non-Hispanic; OR, odds ratio; PUMA, Public Use Microdata Area; ref, reference level.

[a] Adjusted for year, maternal age and education, and PUMA-level poverty and proportion of residents who are non-Hispanic Black.

[b] Tertile 1 indicates low structural racism, tertile 3 indicates high structural racism.

[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 high concentration of privilege.

[d] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.

[e] Excluded 7 PUMAs: 3810, 3901, 4017, 4103, 4104, 4108, and 4109 with 1,945 births, and another 286 stillbirths with reported birthweight <150g.

[f] Excluded 8 PUMAs: 3708, 3709, 3710, 4007, 4010, 4105, 4107, and 4113 with 5,992 births, and another 265 stillbirths with reported birthweight <150g.

[g] Excluded 14 PUMAs: 3801, 3805, 3808, 3809, 3810, 3901, 4017, 4102, 4103, 4104, 4107, 4108, 4109, and 4110 with 7,147 births, and another 282 stillbirths with reported birthweight <150g.

[h] Excluded 18 PUMAs: 3702, 3704, 3705, 3707, 3708, 3709, 3710, 3802, 4002, 4007, 4008, 4010, 4102, 4104, 4105, 4107, 4112, and 4113 with 17,640 births, and another 257 stillbirths with reported birthweight <150g.

Table A28: Sensitivity analysis 5: Interaction assessment for stratification by vintage: Odds ratios for associations between four structural racism measures and stillbirth, comparing models with and without terms for interaction between structural racism and race, in non-Hispanic Black and white births, 2009-2013 (vintage 2013) and 2013-2018 (vintage 2018), NYC

	ACS Vintage 2013 (n=278,240)			ACS Vintage 2018 (n=268,743)		
	No interaction, OR (95% CI) [a]	Interaction, OR (95% CI) [a, e]	*P* value [f]	No interaction, OR (95% CI) [a]	Interaction, OR (95% CI) [a, e]	*P* value [f]
Index of Dissimilarity						
Continuous [d]						
Dissimilarity	1.08 (0.99, 1.18)	1.06 (0.93, 1.20)		1.05 (1.00, 1.11)	1.05 (0.95, 1.15)	
white	ref	ref		ref	ref	
Black	1.79 (1.54, 2.08)	1.77 (1.51, 2.07)		2.04 (1.79, 2.32)	2.04 (1.79, 2.32)	
Black*Dissimilarity		1.04 (0.90, 1.20)	<0.61		1.01 (0.89, 1.13)	<0.93
Categorical						
Tertile 1 [b]	ref	ref		ref	ref	
Tertile 2	1.06 (0.84, 1.33)	0.96 (0.71, 1.29)		1.07 (0.95, 1.21)	0.99 (0.81, 1.21)	
Tertile 3 [b]	1.24 (1.00, 1.52)	1.11 (0.82, 1.51)		1.16 (1.03, 1.30)	1.10 (0.92, 1.33)	
white	ref	ref		ref	ref	
Black	1.80 (1.55, 2.09)	1.58 (1.20, 2.08)		2.06 (1.81, 2.34)	1.92 (1.57, 2.35)	
Black*Tertile 2		1.20 (0.84, 1.71)	<0.33		1.13 (0.88, 1.45)	<0.35
Black*Tertile 3 [b]		1.18 (0.84, 1.65)	<0.35		1.08 (0.84, 1.39)	<0.54
Index of Isolation						
Continuous [d]						
Isolation	0.94 (0.78, 1.13)	0.98 (0.81, 1.18)		1.01 (0.91, 1.13)	1.08 (0.96, 1.20)	
white	ref	ref		ref	ref	
Black	1.83 (1.56, 2.14)	1.90 (1.62, 2.22)		2.05 (1.77, 2.36)	2.19 (1.90, 2.51)	
Black*Isolation		0.81 (0.69, 0.96)	<0.02		0.76 (0.66, 0.87)	<0.01
Categorical						
Tertile 1 [b]	ref	ref		ref	ref	
Tertile 2	0.86 (0.64, 1.14)	0.88 (0.64, 1.22)		1.00 (0.84, 1.19)	1.14 (0.93, 1.40)	
Tertile 3 [b]	0.96 (0.60, 1.53)	1.23 (0.75, 2.02)		0.94 (0.72, 1.23)	1.12 (0.83, 1.53)	
white	ref	ref		ref	ref	
Black	1.83 (1.56, 2.14)	2.63 (1.97, 3.53)		2.07 (1.80, 2.38)	3.54 (2.72, 4.61)	
Black*Tertile 2		0.71 (0.48, 1.04)	<0.08		0.51 (0.36, 0.72)	<0.01
Black*Tertile 3 [b]		0.54 (0.37, 0.79)	<0.01		0.49 (0.35, 0.68)	<0.01
Educational Inequity Ratio						
Continuous [d]						
Educational Inequity	1.10 (1.00, 1.20)	1.04 (0.92, 1.17)		1.03 (0.98, 1.08)	1.02 (0.95, 1.10)	
white	ref	ref		ref	ref	
Black	1.80 (1.55, 2.10)	1.83 (1.57, 2.14)		2.06 (1.81, 2.35)	2.06 (1.81, 2.35)	
Black* Educational Inequity		1.10 (0.95, 1.27)	<0.19		1.02 (0.92, 1.12)	<0.76
Categorical						
Tertile 1 [b]	ref	ref		ref	ref	
Tertile 2	0.87 (0.69, 1.09)	0.95 (0.69, 1.31)		1.02 (0.91, 1.15)	1.10 (0.90, 1.35)	
Tertile 3 [b]	0.81 (0.65, 1.00)	0.98 (0.74, 1.31)		0.95 (0.84, 1.06)	0.94 (0.78, 1.15)	
white	ref	ref		ref	ref	
Black	1.80 (1.54, 2.09)	2.27 (1.71, 3.02)		2.04 (1.79, 2.33)	2.09 (1.72, 2.54)	
Black*Tertile 2		0.82 (0.56, 1.21)	<0.32		0.89 (0.69, 1.15)	<0.39
Black*Tertile 3 [b]		0.69 (0.49, 0.97)	<0.03		1.01 (0.79, 1.29)	<0.93
Index of Concentration at the Extremes						
Continuous [d]						
ICE	1.23 (0.89, 1.69)	1.19 (0.86, 1.63)		1.04 (0.88, 1.23)	1.00 (0.85, 1.18)	
white	ref			ref		
Black	1.83 (1.57, 2.13)	1.85 (1.59, 2.15)		2.08 (1.82, 2.37)	2.13 (1.87, 2.42)	
Black*ICE		1.20 (1.03, 1.39)	<0.02		1.24 (1.09, 1.40)	<0.01

	ACS Vintage 2013 (n=278,240)			ACS Vintage 2018 (n=268,743)		
	No interaction, OR (95% CI) [a]	Interaction, OR (95% CI) [a, e]	*P* value [f]	No interaction, OR (95% CI) [a]	Interaction, OR (95% CI) [a, e]	*P* value [f]
Categorical						
Quintile 1 [c]	ref	ref		ref	ref	
Quintile 2	1.43 (1.03, 2.00)	1.05 (0.59, 1.84)		1.04 (0.88, 1.23)	0.86 (0.59, 1.25)	
Quintile 3	1.80 (1.15, 2.81)	1.61 (0.92, 2.80)		1.21 (0.93, 1.58)	0.82 (0.54, 1.25)	
Quintile 4	1.93 (1.15, 3.25)	1.57 (0.87, 2.82)		1.24 (0.90, 1.70)	0.81 (0.54, 1.22)	
Quintile 5 [c]	2.51 (1.24, 5.08)	1.96 (0.92, 4.15)		1.21 (0.83, 1.76)	0.81 (0.52, 1.28)	
white	ref	ref		ref	ref	
Black	1.85 (1.58, 2.16)	1.50 (1.09, 2.05)		2.12 (1.84, 2.43)	1.43 (1.06, 1.93)	
Black*Quintile 2		1.42 (0.86, 2.35)	<0.17		1.20 (0.81, 1.78)	<0.37
Black*Quintile 3		1.08 (0.70, 1.65)	<0.74		1.56 (1.04, 2.34)	<0.03
Black*Quintile 4		1.31 (0.82, 2.08)	<0.26		2.29 (1.46, 3.60)	<0.01
Black*Quintile 5 [c]		1.80 (1.09, 2.97)	<0.02		2.00 (1.30, 3.08)	<0.01

Abbreviations: ACS, American Community Survey; CI, confidence interval; ICE, Index of Concentration at the Extremes; OR, odds ratio; ref, reference level.

[a] Adjusted for year, maternal age, education, and race, proportion of the PUMA population under the poverty line, and proportion of PUMA residents who are non-Hispanic Black.

[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.

[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

[d] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.

[e] Interaction models included terms for interaction between the structural racism measure and race (NH Black, NH white).

[f] P values for cross-product terms from the Wald test.

Table A29: Sensitivity analysis 5: Stratification by vintage for exposures showing evidence of interaction with race: Odds ratios for associations between three structural racism measures and stillbirth in non-Hispanic Black and white births in NYC in 2009-2013 (vintage 2013) and 2013-2018 (vintage 2018)

	ACS Vintage 2013, OR (95% CI) [d]		ACS Vintage 2018, OR (95% CI) [d]	
	NH Black	NH white	NH Black	NH white
n	119,487	158,753	124,586	198,906
Index of Isolation				
Continuous [c]	0.85 (0.68, 1.08)	0.90 (0.67, 1.23)	0.72 (0.60, 0.88)	1.07 (0.92, 1.25)
Categorical				
Tertile 1 [a]	ref	ref	ref	ref
Tertile 2	0.66 (0.45, 0.96)	0.90 (0.58, 1.40)	0.57 (0.43, 0.75)	1.06 (0.83, 1.34)
Tertile 3 [a]	0.70 (0.42, 1.16)	1.52 (0.59, 3.92)	0.56 (0.38, 0.82)	0.87 (0.49, 1.53)
Index of Concentration at the Extremes				
Continuous [c]	1.39 (0.96, 2.03)	1.35 (0.82, 2.23)	1.41 (1.08, 1.86)	1.01 (0.82, 1.24)
Categorical				
Quintile 1 [b]	ref	ref	ref	ref
Quintile 2	1.38 (0.99, 1.91)	1.34 (0.61, 2.94)	1.05 (0.86, 1.28)	0.84 (0.58, 1.23)
Quintile 3	1.58 (1.01, 2.47)	2.35 (0.92, 5.99)	1.32 (0.95, 1.83)	0.83 (0.50, 1.38)
Quintile 4	1.79 (1.00, 3.18)	2.91 (0.97, 8.74)	2.07 (1.34, 3.20)	0.80 (0.44, 1.44)
Quintile 5 [b]	2.88 (1.31, 6.36)	4.11 (1.02, 16.58)	1.80 (1.09, 2.96)	0.77 (0.41, 1.48)
Educational Inequity Ratio				
Continuous [c]	1.10 (0.99, 1.22)	1.09 (0.93, 1.27)	1.04 (0.95, 1.14)	1.04 (0.96, 1.13)
Categorical				
Tertile 1 [a]	ref	ref	ref	ref
Tertile 2	0.86 (0.65, 1.13)	0.89 (0.59, 1.33)	0.90 (0.74, 1.11)	1.14 (0.93, 1.41)
Tertile 3 [a]	0.76 (0.59, 0.98)	0.90 (0.62, 1.31)	0.91 (0.74, 1.11)	0.92 (0.76, 1.11)

Abbreviations: ACS, American Community Survey; CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.

[a] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.

[b] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

[c] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.

[d] Adjusted for year, maternal age, education, proportion of the PUMA population under the poverty line, and proportion of PUMA residents who are non-Hispanic Black.

Table A30: Sensitivity analysis 6: Single year assessment: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and white births in NYC in four years: 2009, 2016, 2011, 2018

	2009, OR (95% CI) [d]		2016, OR (95% CI) [d]		2011, OR (95% CI) [d]		2018, OR (95% CI) [d]	
	NH Black	NH white	NH Black	NH white	NH Black	NH white	NH Black	NH white
n	25,493	31,271	20,424	33,397	24,043	31,735	19,101	33,105
Index of Isolation								
Continuous [c]	1.83 (0.85, 3.92)	0.81 (0.39, 1.68)	0.88 (0.58, 1.34)	1.00 (0.65, 1.53)	0.77 (0.56, 1.07)	0.97 (0.64, 1.46)	0.81 (0.54, 1.22)	1.19 (0.78, 1.81)
Categorical								
Tertile 1 [a]	ref	ref	ref	ref	ref	ref	ref	ref
Tertile 2	1.39 (0.39, 4.97)	1.09 (0.37, 3.23)	0.91 (0.45, 1.87)	1.07 (0.56, 2.03)	0.48 (0.27, 0.83)	0.91 (0.49, 1.69)	0.93 (0.45, 1.93)	1.20 (0.63, 2.29)
Tertile 3 [a]	2.34 (0.42, 12.96)	6.01 (0.42, 85.50)	0.70 (0.28, 1.75)	1.05 (0.21, 5.35)	0.41 (0.21, 0.80)	1.02 (0.26, 4.10)	0.91 (0.37, 2.23)	0.88 (0.20, 3.88)
Index of Concentration at the Extremes								
Continuous [c]	0.80 (0.22, 2.93)	1.15 (0.34, 3.91)	1.41 (0.78, 2.55)	0.86 (0.51, 1.46)	1.64 (0.97, 2.77)	2.17 (1.16, 4.05)	1.63 (0.90, 2.97)	0.97 (0.56, 1.67)
Categorical								
Quint 1 [b]	ref	ref	ref	ref	ref	ref	ref	ref
Quint 2	4.20 (1.49, 11.81)	1.00 (0.11, 9.01)	0.98 (0.64, 1.51)	0.86 (0.26, 2.79)	1.02 (0.70, 1.50)	1.49 (0.48, 4.57)	1.64 (1.03, 2.61)	0.76 (0.30, 1.92)
Quint 3	3.38 (0.89, 12.92)	2.43 (0.22, 26.76)	2.06 (1.06, 4.00)	0.86 (0.19, 3.96)	1.02 (0.59, 1.79)	2.83 (0.76, 10.53)	1.86 (0.85, 4.08)	0.37 (0.10, 1.31)
Quint 4	2.60 (0.46, 14.83)	2.91 (0.17, 49.44)	1.42 (0.49, 4.12)	1.14 (0.20, 6.47)	0.84 (0.36, 1.97)	4.90 (1.01, 23.66)	3.04 (1.00, 9.24)	0.26 (0.06, 1.11)
Quint 5 [b]	2.70 (0.21, 34.31)	1.75 (0.05, 61.66)	1.31 (0.43, 3.99)	0.86 (0.13, 5.43)	2.70 (0.98, 7.45)	6.38 (0.96, 42.31)	4.74 (1.51, 14.92)	0.21 (0.04, 1.01)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; Quint, quintile; ref, reference level.
[a] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[b] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[c] ORs for continuous measures represent change in odds of stillbirth with a 1 standard deviation increase in the structural racism measure.
[d] Adjusted for maternal age, education, proportion of the PUMA population under the poverty line, and proportion of PUMA residents who are non-Hispanic Black.

Table A31: Odds ratios for associations between two structural racism measures and stillbirth, comparing models with and without terms for interaction between structural racism and maternal age, 221,925 non-Hispanic Black births, NYC (2009-2018)

	No interaction, OR (95% CI) [c]	Interaction, [d] OR (95% CI) [c]	*P* value [e]
Isolation			
Tertile 1 [a]	ref	ref	<0.14
Tertile 2	0.61 (0.47, 0.80)	0.56 (0.41, 0.76)	
Tertile 3 [a]	0.60 (0.42, 0.86)	0.60 (0.41, 0.87)	
age	1.14 (1.10, 1.19)	1.26 (1.07, 1.48)	
age squared	1.03 (1.00, 1.06)	1.01 (0.89, 1.14)	
age*Tertile 2		0.96 (0.80, 1.15)	
age*Tertile 3 [a]		0.89 (0.75, 1.05)	
age squared*Tertile 2		1.08 (0.94, 1.24)	
age squared*Tertile 3 [a]		1.01 (0.89, 1.14)	
ICE			
Quintile 1 [b]	ref	ref	<0.07
Quintile 2	1.12 (0.95, 1.33)	1.16 (0.96, 1.40)	
Quintile 3	1.27 (0.95, 1.70)	1.13 (0.83, 1.54)	
Quintile 4	1.70 (1.16, 2.49)	2.07 (1.36, 3.16)	
Quintile 5 [b]	1.90 (1.20, 2.99)	1.80 (1.10, 2.92)	
age	1.14 (1.10, 1.19)	1.11 (1.05, 1.17)	
age squared	1.03 (1.00, 1.06)	1.02 (0.98, 1.07)	
age*Quintile 2		1.04 (0.95, 1.14)	
age*Quintile 3		1.10 (0.98, 1.24)	
age*Quintile 4		0.99 (0.80, 1.23)	
age*Quintile 5 [b]		1.14 (0.95, 1.38)	
age squared*Quintile 2		0.98 (0.91, 1.05)	
age squared*Quintile 3		1.10 (1.01, 1.21)	
age squared*Quintile 4		0.83 (0.69, 1.00)	
age squared*Quintile 5 [b]		1.05 (0.91, 1.20)	

Abbreviations: CI, confidence interval; ICE, Index of Concentration at the Extremes; OR, odds ratio; ref, reference level.

[a] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.

[b] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

[c] Adjusted for year, proportion of the PUMA population under the poverty line, proportion of PUMA residents who are non-Hispanic Black, and maternal education.

[d] Model with interaction includes interaction terms between structural racism measure and age (both Z score and age squared).

[e] P values for the X^2 test for comparison of models with and without interaction terms.

Table A32: Sensitivity analysis: Odds ratios (95% CI) for associations between ICE and stillbirth stratified by maternal age in non-Hispanic Black and non-Hispanic White births, NYC (2009-2018)

	Main model, OR (95% CI) [c]		Additionally adjusted for PUMA % HS, OR (95% CI) [d]	
	NH Black (n=221,925)	NH white (n=325,057)	NH Black (n=221,925)	NH white (n=325,057)
Maternal age 10-19 years				
n	14,389	3,843	14,389	3,843
Quintile 1 [b]	ref	ref	ref	ref
Quintile 2	1.14 (0.67, 1.94)	1.08 (0.06, 18.22)	1.08 (0.63, 1.88)	1.11 (0.06, 19.51)
Quintile 3	1.42 (0.63, 3.22)	0.63 (0.02, 24.80)	1.15 (0.44, 3.04)	0.69 (0.01, 34.36)
Quintile 4	1.07 (0.32, 3.57)	0.73 (0.01, 43.12)	0.80 (0.20, 3.27)	0.84 (0.01, 90.47)
Quintile 5 [b]	1.42 (0.34, 5.90)	0.93 (0.01, 107.42)	0.98 (0.18, 5.38)	1.09 (0.00, 246.87)
Maternal age 20-34 years				
n	160,753	226,235	160,753	226,235
Quintile 1 [b]	ref	ref	ref	ref
Quintile 2	1.07 (0.88, 1.30)	1.07 (0.67, 1.71)	1.07 (0.88, 1.31)	1.06 (0.66, 1.70)
Quintile 3	1.12 (0.82, 1.55)	1.18 (0.63, 2.22)	1.14 (0.79, 1.64)	1.14 (0.59, 2.21)
Quintile 4	1.78 (1.17, 2.72)	1.09 (0.52, 2.29)	1.82 (1.12, 2.97)	1.03 (0.46, 2.30)
Quintile 5 [b]	1.67 (1.00, 2.80)	1.30 (0.56, 2.99)	1.72 (0.93, 3.20)	1.21 (0.48, 3.03)
Maternal age 35-63 years				
n	46,783	94,979	46,783	94,979
Quintile 1 [b]	ref	ref	ref	ref
Quintile 2	1.30 (0.98, 1.72)	0.86 (0.47, 1.57)	1.40 (1.05, 1.86)	0.85 (0.47, 1.56)
Quintile 3	1.73 (1.13, 2.60)	0.95 (0.43, 2.08)	2.20 (1.36, 3.57)	0.92 (0.41, 2.04)
Quintile 4	1.51 (0.79, 2.88)	1.24 (0.51, 3.01)	2.06 (1.01, 4.20)	1.16 (0.46, 2.94)
Quintile 5 [b]	2.70 (1.32, 5.48)	1.30 (0.48, 3.55)	4.21 (1.83, 9.67)	1.20 (0.41, 3.46)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[b] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[c] Main model; adjusted for year, proportion of the PUMA population under the poverty line, proportion of PUMA residents who are non-Hispanic Black, and maternal education. Repeated here from Table 6 for convenience.
[d] Additionally adjusted for proportion of PUMA residents who are 25 years or older with at least a GED or high school diploma.

Table A33: Post-hoc analysis 1a: Stratification by median PUMA % poverty: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	**NH white (n=325,058)**
Index of Isolation		
< Median, PUMA % poverty [d]	n=75,644	n=196,790
Tertile 1 [b]	ref	ref
Tertile 2	0.67 (0.50, 0.91)	1.05 (0.77, 1.42)
Tertile 3 [b]	0.81 (0.50, 1.32)	1.06 (0.45, 2.50)
Median +, PUMA % poverty [d]	n=146,281	n=128,268
Tertile 1 [b]	ref	ref
Tertile 2	0.63 (0.42, 0.95)	1.17 (0.76, 1.81)
Tertile 3 [b]	0.61 (0.39, 0.96)	1.78 (0.92, 3.45)
Index of Concentration at the Extremes		
< Median, PUMA % poverty [d]	n=75,644	n=196,790
Quintile 1 [c]	ref	ref
Quintile 2	1.21 (0.82, 1.76)	0.99 (0.31, 3.16)
Quintile 3	1.24 (0.68, 2.27)	1.03 (0.26, 4.08)
Quintile 4	1.49 (0.73, 3.05)	1.20 (0.27, 5.28)
Quintile 5 [c]	1.60 (0.78, 3.29)	1.11 (0.25, 4.90)
Median +, PUMA % poverty [d]	n=146,281	n=128,268
Quintile 1 [c]	ref	ref
Quintile 2	0.95 (0.77, 1.15)	0.81 (0.53, 1.25)
Quintile 3	1.13 (0.81, 1.57)	0.84 (0.47, 1.50)
Quintile 4	1.51 (0.94, 2.43)	0.70 (0.36, 1.38)
Quintile 5 [c]	1.83 (0.32, 10.62)	0.70 (0.28, 1.77)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion of residents who are non-Hispanic Black.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[d] < Median: 32 PUMAs; Median+: 33 PUMAs

Table A34: Post-hoc analysis 1b: Stratification by median PUMA % Black: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	**NH white (n=325,058)**
Index of Isolation		
< Median, PUMA % Black [d]	n=22,210	n=253,332
Tertile 1 [b]	ref	ref
Tertile 2	0.56 (0.38, 0.84)	0.96 (0.73, 1.26)
Tertile 3 [b]	n/a	n/a
Median +, PUMA % Black [d]	n=199,715	n=71,726
Tertile 1 [b]	ref	ref
Tertile 2	n/a	n/a
Tertile 3 [b]	1.06 (0.89, 1.25)	1.11 (0.83, 1.49)
Index of Concentration at the Extremes		
< Median, PUMA % Black [d]	n=22,210	n=253,332
Quintile 1 [c]	ref	ref
Quintile 2	n/a	n/a
Quintile 3	1.71 (0.56, 5.19)	4.16 (0.49, 35.20)
Quintile 4	2.29 (0.76, 6.92)	4.37 (0.52, 36.47)
Quintile 5 [c]	4.98 (1.40, 17.66)	5.32 (0.63, 45.16)
Median +, PUMA % Black [d]	n=199,715	n=71,726
Quintile 1 [c]	ref	ref
Quintile 2	1.04 (0.90, 1.21)	0.91 (0.64, 1.28)
Quintile 3	1.06 (0.84, 1.33)	1.00 (0.66, 1.50)
Quintile 4	1.35 (0.72, 2.55)	1.65 (0.74, 3.68)
Quintile 5 [c]	0.87 (0.42, 1.78)	0.88 (0.38, 2.00)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level percent poverty.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[d] < Median: 28 PUMAs; Median +: 27 PUMAs

Table A35: Post-hoc analysis 1c: Stratification by median PUMA % Educational Attainment: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	**NH white (n=325,058)**
Index of Isolation		
< Median, PUMA % Educational attainment [d]	n=128,392	n=103,846
Tertile 1 [b]	ref	ref
Tertile 2	0.37 (0.25, 0.57)	0.73 (0.47, 1.13)
Tertile 3 [b]	0.37 (0.22, 0.63)	0.49 (0.20, 1.22)
Median +, PUMA % Educational attainment [d]	n=93,533	n=221,212
Tertile 1 [b]	ref	ref
Tertile 2	0.85 (0.65, 1.11)	1.38 (1.01, 1.89)
Tertile 3 [b]	0.85 (0.59, 1.21)	2.20 (1.15, 4.21)
Index of Concentration at the Extremes		
< Median, PUMA % Educational attainment [d]	n=128,392	n=103,846
Quintile 1 [c]	ref	ref
Quintile 2	1.22 (0.97, 1.52)	1.04 (0.56, 1.94)
Quintile 3	1.27 (0.86, 1.89)	0.86 (0.39, 1.92)
Quintile 4	2.24 (1.30, 3.87)	1.04 (0.46, 2.37)
Quintile 5 [c]	9.07 (3.84, 21.42)	1.88 (0.70, 5.05)
Median +, PUMA % Educational attainment [d]	n=93,533	n=221,212
Quintile 1 [c]	ref	ref
Quintile 2	1.01 (0.79, 1.30)	0.92 (0.54, 1.57)
Quintile 3	1.20 (0.79, 1.80)	1.68 (0.75, 3.75)
Quintile 4	1.25 (0.72, 2.17)	1.46 (0.53, 4.07)
Quintile 5 [c]	1.23 (0.67, 2.25)	1.36 (0.47, 3.93)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion non-Hispanic Black and percent poverty.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[d] < Median: 30 PUMAs; Median +: 29 PUMAs

Table A36: Post-hoc analysis 1d: Stratification by sex: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]	OR (95% CI) [d]	OR (95% CI) [d]
	NH Black (n=221,925)	NH white (n=325,058)	NH Black (n=221,925)	NH white (n=325,058)
Index of Isolation				
Male	n=112,680	n=167,562	n=112,680	n=167,562
Tertile 1 [b]	ref	ref	ref	ref
Tertile 2	0.71 (0.51, 1.00)	1.16 (0.82, 1.65)	0.66 (0.46, 0.93)	1.23 (0.84, 1.78)
Tertile 3 [b]	0.79 (0.51, 1.21)	2.01 (0.95, 4.22)	0.68 (0.43, 1.07)	2.41 (1.10, 5.31)
Female	n=108,792	n=157,186	n=108,792	n=157,186
Tertile 1 [b]	ref	ref	ref	ref
Tertile 2	0.67 (0.45, 0.99)	0.93 (0.64, 1.36)	0.61 (0.40, 0.92)	0.95 (0.64, 1.40)
Tertile 3 [b]	0.67 (0.40, 1.11)	0.86 (0.38, 1.95)	0.56 (0.32, 0.96)	0.99 (0.43, 2.32)
Index of Concentration at the Extremes				
Male	n=112,680	n=167,562	n=112,680	n=167,562
Quintile 1 [c]	ref	ref	ref	ref
Quintile 2	1.12 (0.90, 1.38)	0.84 (0.47, 1.50)	1.02 (0.81, 1.28)	0.77 (0.42, 1.44)
Quintile 3	1.27 (0.91, 1.77)	0.95 (0.45, 2.01)	1.16 (0.80, 1.67)	1.07 (0.49, 2.35)
Quintile 4	1.71 (1.08, 2.71)	0.95 (0.40, 2.26)	1.57 (0.96, 2.57)	1.01 (0.40, 2.52)
Quintile 5 [c]	2.08 (1.20, 3.58)	0.99 (0.37, 2.63)	1.84 (1.02, 3.31)	0.97 (0.35, 2.75)
Female	n=108,792	n=157,186	n=108,792	n=157,186
Quintile 1 [c]	ref	ref	ref	ref
Quintile 2	1.09 (0.85, 1.41)	0.95 (0.54, 1.68)	1.03 (0.78, 1.35)	1.13 (0.63, 2.04)
Quintile 3	1.35 (0.89, 2.05)	1.16 (0.54, 2.49)	1.22 (0.78, 1.91)	1.35 (0.61, 2.99)
Quintile 4	1.61 (0.91, 2.83)	1.02 (0.42, 2.48)	1.53 (0.83, 2.80)	1.18 (0.47, 2.97)
Quintile 5 [c]	1.37 (0.68, 2.76)	1.24 (0.45, 3.38)	1.37 (0.65, 2.87)	1.43 (0.50, 4.05)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion non-Hispanic Black and percent poverty.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.
[d] Additionally adjusted for maternal medical conditions, number of prenatal care visits, and insurance status.

Table A37: Post-hoc analysis 1e: Stratification by gestational age: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	**NH white (n=325,058)**
Index of Isolation		
Preterm (20-36 weeks)	n=25,997	n=16,420
Tertile 1 [b]	ref	ref
Tertile 2	0.54 (0.41, 0.72)	1.00 (0.74, 1.36)
Tertile 3 [b]	0.57 (0.39, 0.83)	1.00 (0.55, 1.83)
Term (37+ weeks)	n=195,928	n=308,638
Tertile 1 [b]	ref	ref
Tertile 2	1.11 (0.62, 1.99)	0.76 (0.50, 1.17)
Tertile 3 [b]	1.13 (0.55, 2.29)	1.37 (0.52, 3.64)
Index of Concentration at the Extremes		
Preterm (20-36 weeks)	n=25,997	n=16,420
Quintile 1 [c]	ref	ref
Quintile 2	1.08 (0.89, 1.32)	1.20 (0.77, 1.88)
Quintile 3	1.14 (0.82, 1.59)	1.36 (0.76, 2.42)
Quintile 4	1.67 (1.08, 2.60)	1.80 (0.92, 3.55)
Quintile 5 [c]	1.92 (1.14, 3.23)	1.97 (0.91, 4.26)
Term (37+ weeks)	n=195,928	n=308,638
Quintile 1 [c]	ref	ref
Quintile 2	1.16 (0.81, 1.66)	1.01 (0.50, 2.04)
Quintile 3	1.26 (0.73, 2.17)	1.13 (0.45, 2.82)
Quintile 4	1.43 (0.66, 3.09)	1.30 (0.46, 3.71)
Quintile 5 [c]	0.86 (0.31, 2.33)	1.90 (0.59, 6.09)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion non-Hispanic Black and percent poverty.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

Table A38: Post-hoc analysis 2: Additional adjustment for individual-level covariates: Odds ratios for associations between two structural racism measures and stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	NH white (n=325,058)
Index of Isolation		
Tertile 1 [b]	ref	ref
Tertile 2	0.57 (0.44, 0.75)	1.05 (0.80, 1.38)
Tertile 3 [b]	0.52 (0.36, 0.76)	1.41 (0.82, 2.43)
Index of Concentration at the Extremes		
Quintile 1 [c]	ref	ref
Quintile 2	1.03 (0.86, 1.23)	1.03 (0.69, 1.54)
Quintile 3	1.11 (0.82, 1.52)	1.24 (0.72, 2.13)
Quintile 4	1.48 (0.98, 2.24)	1.24 (0.66, 2.33)
Quintile 5 [c]	1.68 (1.03, 2.73)	1.37 (0.67, 2.78)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion non-Hispanic Black and percent poverty, and maternal medical conditions, number of prenatal care visits, and insurance status.
[b] Tertile 1 indicates low isolation, tertile 3 indicates high isolation.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

Table A39: Post-hoc analysis 3a: ICE for poverty only [b]: Odds ratios for associations with stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	NH white (n=325,058)
Quintile 1 [c]	ref	ref
Quintile 2	1.19 (0.94, 1.52)	0.79 (0.58, 1.08)
Quintile 3	1.30 (0.98, 1.72)	0.92 (0.64, 1.32)
Quintile 4	1.48 (1.04, 2.12)	1.33 (0.89, 1.98)
Quintile 5 [c]	1.40 (0.87, 2.27)	1.26 (0.77, 2.08)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion non-Hispanic Black and percent poverty.
[b] Source of data for this exposure: ACS Table B19101: Family income in the past 12 months, in inflation-adjusted dollars, Universe: Families (vs ICE original which used households with <$25,000 and $100,000+, with race id'd). Vintages 2013 and 2018.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

Table A40: Post-hoc analysis 3b: ICE for race only [b]: Odds ratios for associations with stillbirth in non-Hispanic Black and non-Hispanic white births, NYC (2009-2018)

	OR (95% CI) [a]	OR (95% CI) [a]
	NH Black (n=221,925)	NH white (n=325,058)
Quintile 1 [c]	ref	ref
Quintile 2	0.94 (0.73, 1.22)	1.23 (0.77, 1.99)
Quintile 3	1.11 (0.77, 1.60)	1.37 (0.74, 2.54)
Quintile 4	1.53 (0.95, 2.46)	1.34 (0.62, 2.88)
Quintile 5 [c]	1.45 (0.87, 2.41)	1.44 (0.66, 3.14)

Abbreviations: CI, confidence interval; NH, non-Hispanic; OR, odds ratio; ref, reference level.
[a] Adjusted for year, maternal age and education, and PUMA-level proportion non-Hispanic Black and percent poverty.
[b] Source of data for this exposure: ACS Table B03002: Hispanic or Latino Origin by Race, Universe: Total population (vs ICE original which used non-Hispanic white and Black [sic] households with income levels id'd). Including only non-Hispanic white and non-Hispanic Black. Vintages 2013 and 2018.
[c] Quintile 1 indicates high concentration of disadvantage, Quintile 5 indicates high concentration of privilege.

Table A41: Massey and Denton's five domains of residential segregation

Domain	Answers the question:
1. Evenness	How evenly distributed are the individuals of one race across neighborhoods?
2. Exposure	How likely is it that individuals of different races will encounter each other?
3. Centralization	To what degree do individuals of one race live in the area considered most 'central'?
4. Concentration	How much land area do individuals of one race occupy relative to their population?
5. Clustering	How closely located are neighborhoods that are mostly populated by individuals of a particular race?

Table A42: Recommended measures of segregation

Domain	Measure	Massey and Denton recommended (MD)? Used by U.S. Census (USC)?	Formula	Definitions of variables
Evenness	D, Dissimilarity Index ("new" version)	MD, USC	$\frac{\sum_{i=1}^{n}\left[t_i\left\lvert(p_i - P)\right\rvert\right]}{[2TP(1-P)]}$	▪ n, number of areas (census tracts) in the metropolitan area, ranked smallest to largest by land area ▪ m, number of areas (census tracts) in the metropolitan area, ranked by increasing distance from the Central Business District (m=n) ▪ x_i, the minority population of area i ▪ y_i, the majority population of area i (non-Hispanic white for the U.S. Census report) ▪ y_j, the majority population of area j ▪ t_i, the total population of area i ▪ t_j, the total population of area i ▪ X, the sum of all x_i (the total minority population) ▪ Y, the sum of all y_i (the total majority population) ▪ T, the sum of all t_i (the total population) ▪ p_i, the ratio of x_i to t_i (proportion of area i's population that is minority) ▪ a_i, the land area of area i ▪ A, the sum of all a_i (the total land area) ▪ n1, rank of area where the sum of all t_i from area 1 (smallest in size) up to area n1 is equal to X ▪ T_1, the sum of all t_i in area 1 up to area n ▪ n2, rank of area where the sum of all t_i from area n (largest in size) down to area n2 is equal to X ▪ T_2, the sum of all t_i in area n2 up to area n ▪ d_{ij}, the distance between area i and area j centroids, where $d_{ii} = (0.6a_i)^{0.5}$ ▪ c_{ij}, the exponential transform of d_{ij} [= exp(-d_{ij})]
Exposure	xP*y, Interaction Index	MD	$\sum_{i=1}^{n}\left[\left(\frac{x_i}{X}\right)\left(\frac{y_i}{t_i}\right)\right]$	
	xP*x, Isolation Index	USC	$\sum_{i=1}^{n}\left[\left(\frac{x_i}{X}\right)\left(\frac{x_i}{t_i}\right)\right]$	
Centralization	ACE, Absolute Centralization Index	MD, USC	$\sum_{i=1}^{m}(X_{i-1}A_i) - \sum_{i=1}^{m}(X_iA_{i-1})$	
Concentration	RCO, Relative Concentration Index	MD	$\left\{\left[\frac{\sum_{i=1}^{n}\left(\frac{x_i a_i}{X}\right)}{\sum_{i=1}^{n}\left(\frac{y_i a_i}{Y}\right)}\right] - 1\right\} \Big/ \left\{\left[\frac{\sum_{i=1}^{n1}\left(\frac{t_i a_i}{T_1}\right)}{\sum_{i=n2}^{n}\left(\frac{t_i a_i}{T_2}\right)}\right] - 1\right\}$	
	Delta Index	USC	$0.5\sum_{i=1}^{n}\left\lvert\left(\frac{x_i}{X}\right) - \left(\frac{a_i}{A}\right)\right\rvert$	
Clustering	SP, Spatial Proximity Index	MD, USC	$\frac{(XP_{xx} + YP_{yy})}{TP_{tt}}$ where $P_{gg} = \sum_{i=1}^{n}\sum_{j=1}^{n}\left[\frac{(g_i g_j c_{ij})}{G^2}\right]$ and $\{g,G\} = \{x,X\},\{y,Y\},\{t,T\}$	

These are Massey and Denton's five recommended measures of segregation along with the indices selected by the U.S. Census for its study of segregation 1980-2000.[212 227]

Table A43: Indices used to measure residential segregation in selected studies of adverse pregnancy outcomes

Outcome	Domain	Measure	Level
SINGLE MEASURE USED			
SB[81]	Evenness	Dissimilarity Index (formula not given)	County (from census tracts)
IM[421]	Evenness	Dissimilarity Index (older version)	Metropolitan area (from census tracts)
MULTIPLE MEASURES USED			
PTB[230]	Evenness	Dissimilarity Index (older version)	Metropolitan area (from census tracts)
	Exposure	Interaction Index [a]	
LBW, PTB[237]	Evenness	Dissimilarity Index (newer version)	County (from census tracts)
	Exposure	Isolation Index	
LBW[231]	Evenness	Dissimilarity Index (newer version)	Metropolitan area (from census tracts)
	Centralization	Relative Centralization Index	
SB[64]	Evenness (current and persistent)	Dissimilarity Index (older version)	Hospital reference region (from zip code)
	Exposure (current and persistent)	Isolation Index [b]	
BW, PTB, FGR[209]	Exposure	Isolation Index	Metropolitan area (from census tracts)
	Clustering	Spatial Proximity Index	
GA, BW[199]	Evenness	Dissimilarity Index (older version)	County (from census tracts)
	Exposure	Isolation Index	
	Concentration	Delta Index	
PTB[253]	Evenness	Dissimilarity Index (formula not given)	Unclear; only census tract is mentioned
	Exposure	Isolation Index	
	Exposure	Interaction Index	
COMPOSITE USED			
IM, LBW[240]	Evenness	Dissimilarity Index (newer version)	Metropolitan area (from census tracts)
	Exposure	Isolation Index	
	Concentration	Relative Concentration Index	
	Centralization	Absolute Centralization Index	
	Clustering	Spatial Proximity Index	
	Composite	Equally-weighted average of standardized z-scores of these 5 measures	
PTB[213]	Composite	Hypersegregation (index value >0.60 in at least 4 of 5 domains)	Metropolitan area (from census tracts)
	Evenness [c]	*Dissimilarity Index (formula not given)*	
	Exposure [c]	*Isolation Index*	
	Concentration [c]	*Relative Concentration Index*	
	Centralization [c]	*Absolute Centralization Index*	
	Clustering [c]	*Spatial Proximity Index*	

Abbreviations: BW, birthweight; FGR, fetal growth restriction; GA, gestational age; IM, infant mortality; LBW, low birthweight; PTB, preterm birth; SB, stillbirth.

[a] *Mislabeled as Isolation Index.*

[b] *Isolation Index in this paper has an error: P_T should be p_i*

[c] *Data for individual indices not reported, only used to construct composite.*

Table A44: Lack of 1-to-1 mapping between segregation indices and dimensions, and differential mapping by race/ethnicity

	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Black Americans	Exposure Clustering	Concentration Centralization	Evenness	Clustering	Centralization
Hispanic Americans	Evenness Exposure Clustering	Exposure Concentration Clustering	Concentration Centralization	Centralization	none
Asian Americans	Exposure Concentration Clustering	Evenness Clustering	Centralization	Centralization	Clustering

Dimension is mentioned if oblique rotation factor loading for ≥1 index in that domain was ≥0.50 (data from Tables 6-8 in [422]).

Table A45: Algorithm for coding of maternal risk factors covariates

DOHMH datasets for stillbirths 2009-2010 included:	DOHMH datasets for stillbirths 2011-2018 included:	DOHMH datasets for livebirths 2009-2018 included:	From the available data, we created these 8 covariates:
chronic hypertension	pre-pregnancy hypertension	pre-pregnancy hypertension	1. Chronic hypertension
pregnancy-associated hypertension	gestational hypertension (includes pre-eclampsia)	gestational hypertension	2. Gestational hypertension
preeclampsia			
chronic diabetes	diabetes—pre-pregnancy	diabetes—pre-pregnancy	3. Chronic diabetes
gestational diabetes	gestational diabetes	gestational diabetes	4. Gestational diabetes
genital herpes	HSV	HSV	5. STD
other STD	gonorrhoea	gonorrhoea	
	syphilis	syphilis	
	chlamydia	chlamydia	
hepatitis	hepatitis B	hepatitis B	6. Hepatitis
	hepatitis C	hepatitis C	
cardiac disease	cardiac disease-structural defect	cardiac disease-structural defect	7. Cardiac disease
	cardiac disease-functional defect	cardiac disease-functional defect	
other	other risk factor	n/a	8. Other risk factor
anemia (Hct less than 30/Hgb less than 10)	n/a	anemia	
acute or chronic lung disease	n/a	asthma/acute or chronic lung disease	
hydramnios/oligohydramnios	n/a	oligohydramnios	
	n/a	polyhydramnios	
hemoglobinopathy	n/a	hemoglobinopathy	
eclampsia	n/a	eclampsia	
Rh sensitization	n/a	Rh sensitization	
uterine bleeding trimester-1	n/a	other vaginal bleeding	
uterine bleeding trimester-2	n/a		
uterine bleeding trimester-3	n/a		
previous infant 4000+ grams	n/a	n/a	
previous preterm or small for-gestational-age infant	n/a	n/a	
incompetent cervix	n/a	n/a	
renal disease	n/a	n/a	
n/a	other previous poor pregnancy outcome (spontaneous or induced termination, ectopic pregnancy) not including index pregnancy	other previous poor pregnancy outcome (loss <20 weeks, loss 20+ weeks, induced termination)	
n/a	other serious chronic illness	other serious chronic illness	
n/a	abruptio placenta (but only recorded if an initiating or contributing factor in cause of death)	abruptio placenta	
n/a	fertility drug treatment/artificial/intrauterine insemination	fertility drug treatment/artificial/intrauterine insemination	
n/a	TB	TB	
n/a	rubella	rubella	
n/a	bacterial vaginosis	bacterial vaginosis	
n/a	n/a	pre-labor referral for high-risk care	
n/a	n/a	fetal reduction	

DOHMH datasets for stillbirths 2009-2010 included:	DOHMH datasets for stillbirths 2011-2018 included:	DOHMH datasets for livebirths 2009-2018 included:	From the available data, we created these 8 covariates:
n/a	listeria	n/a	
n/a	group B strep	n/a	
n/a	CMV	n/a	
n/a	parvovirus	n/a	
n/a	toxoplasmosis	n/a	
n/a	other infection in pregnancy	n/a	

Abbreviations: DOHMH, Department of Health and Mental Hygiene; STD, sexually transmitted disease; TB, tuberculosis.
DOHMH provided 10 datasets for livebirths and 10 datasets for stillbirths, one for each year 2009-2018. Data on maternal medical conditions were different for (a) livebirths, (b) stillbirths in 2009-2010, and (c) stillbirths in 2011-2018. In order to construct a merged dataset, it was necessary to align these data. We created 8 maternal medical condition covariates from the available data, including: (1) chronic hypertension, (2) gestational hypertension, (3) chronic diabetes, (4) gestational diabetes, (5) STDs, (6) hepatitis, (7) cardiac disease, and (8) other medical risk factors. This table shows which covariates from the original DOHMH datasets were mapped to each of these 8 new covariates. 'n/a' indicates that the covariate (row) was not available in the datasets (column).

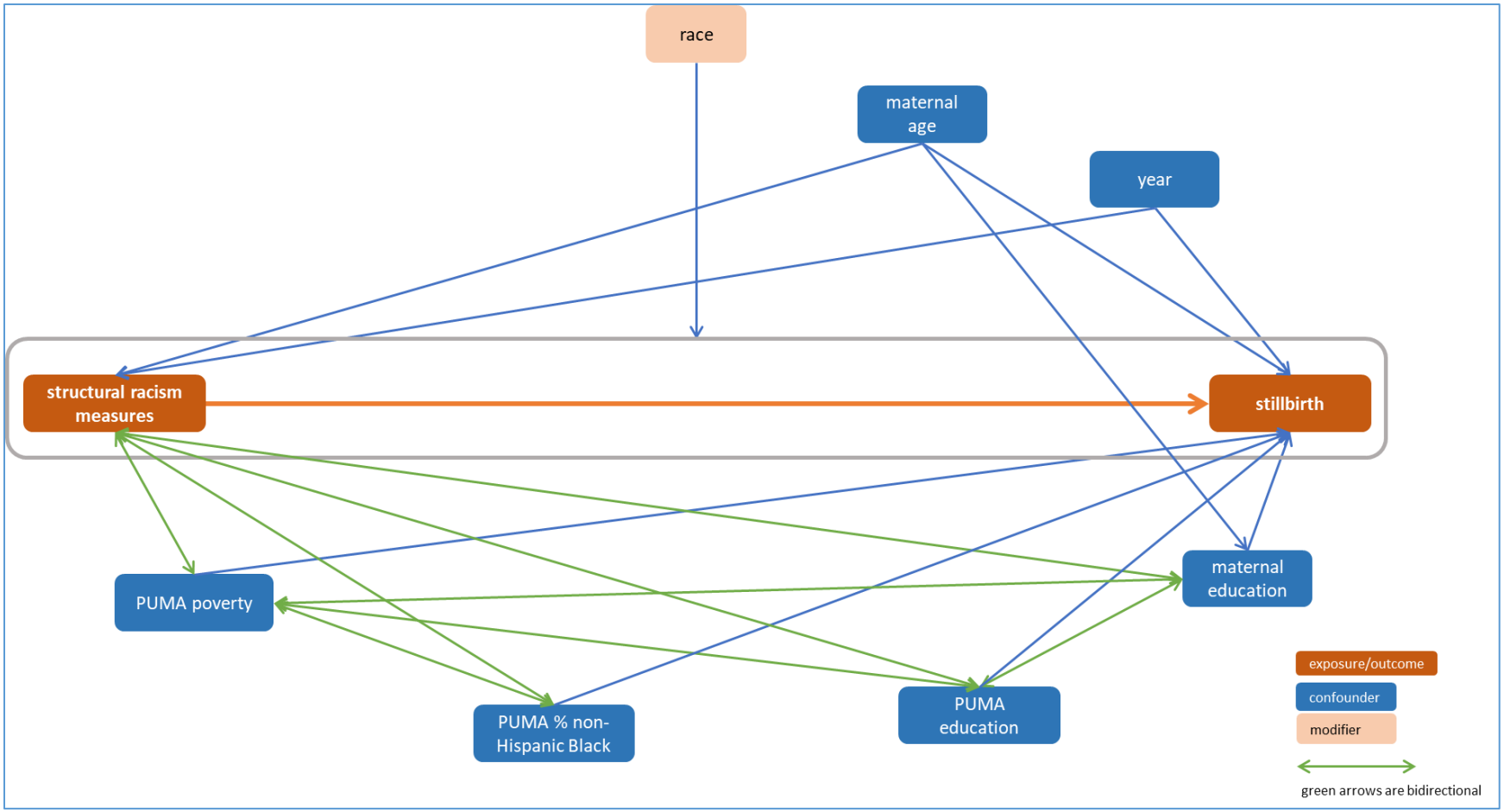


Figure A6: Theoretical diagram of associations between structural racism measures and stillbirth

Abbreviation: PUMA, Public Use Microdata Area.

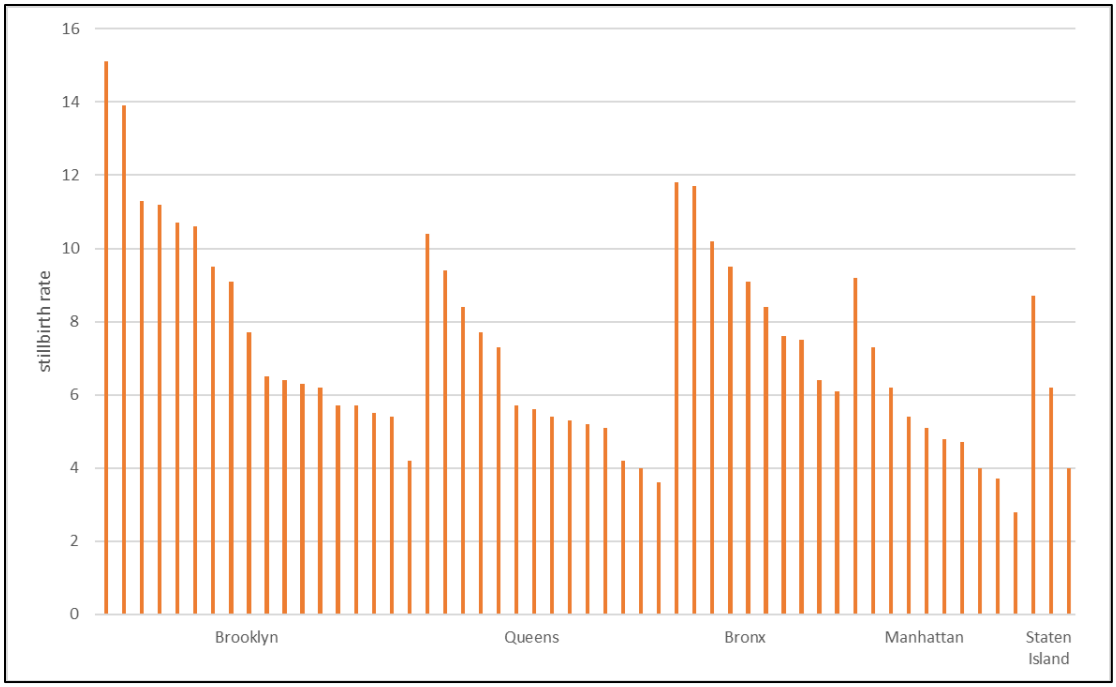


Figure A7: Stillbirth rates in each of NYC's 55 PUMAs, 2009-2018, stratified by borough (n=7,859 stillbirths)

Abbreviation: PUMA, Public Use Microdata Area.
Stillbirth rates calculated as # of stillbirths per 1000 total births.

Additional tables and figures for Chapter 4

Table A46: Distribution of DNA samples from 63 stillbirths and 126 livebirths by site and plate

	Plate 1			Plate 2 [a]			Total		
Site	**livebirths**	**stillbirths**	**Total**	**livebirths**	**stillbirths**	**Total**	**livebirths**	**stillbirths**	**Total**
Brown	18	9	27	18	9	27	36	18	54
Emory	4	2	6	4	2	6	8	4	12
UTMB	8	4	12	8	4	12	16	8	24
UTHSC	12	6	18	12	6	18	24	12	36
Utah	22	11	33	20	10	30	42	21	63
total	64	32	96	62	31	93	126	63	189

Abbreviations: UTHSC, University of Texas Health Sciences Center at San Antonio; UTMB, University of Texas Medical Branch at Galveston.

[a] *Three wells on Plate 2 were empty (as they were not needed).*

Table A47: Predicted proportions of six cell types, [a] n=189 samples

	All		Stillbirths		Livebirths	
	mean	SD	mean	SD	mean	SD
Syncytiotrophoblast	58.8	9.2	55.3	12.0	60.6	6.8
Stromal	14.7	4.7	14.6	6.9	14.8	3.2
Endothelial	10.7	3.7	9.0	4.0	11.5	3.2
Trophoblasts	7.7	4.8	9.5	5.6	6.8	4.0
Hofbauer	4.5	3.6	6.4	5.4	3.6	1.5
nRBC	2.6	4.2	4.4	6.9	1.8	1.2

Abbreviations: nRBC, nucleated red blood cells; SD, standard deviation.
[a] Predicted after the method of Yuan et al.[423]

Table A48: Results of literature search for candidate genes

Date	Search terms	Limits	# reports found [a]
4-15-19	Stress, differential methylation	Title/abstract	14
4-30-19	Microarray, bisulfite sequencing, methylation, stress, placenta	Title/abstract	114
4-30-19	GWAS, stress	Title/abstract	316
5-7-19	Microarray, bisulfite sequencing, methylation, placenta, stillbirth	none	13
5-7-19	GWAS, stillbirth	none	5
5-29-21	Methylation, stress, stillbirth	Title/abstract, English, human, 2010 onward	867, of which 80 relevant and new
5-29-21	Stillbirth, methylation	Humans, English	66, none new
5-29-21	Maternal stress, methylation	Humans, English	43, none new
5-29-21	Stillbirth, epigenetic	Humans, English	19, none new

Abbreviation: GWAS, genome-wide association study.
[a] Searches conducted in PubMed.

Table A49: Details of the five candidate genes: *BDNF, FKBP5, HSD11B2, IGF2, NR3C1*

BDNF

CpGs	Location	Placental expression	Functions (paraphrased from sources as indicated)		
93 interrogated by 850k microarray	11p14.1; 12 exons	moderate; also positive evidence from [297]; but very low per Genecards	"codes for brain-derived neurotrophic factor, a growth factor involved in neural development, cell differentiation, and synaptic plasticity. Present in both the brain and periphery, *BDNF* plays critical roles throughout the body and is **essential for placental and fetal development**… During the prenatal period, *BDNF* **potentiates placental development** and facilitates cytotrophoblast differentiation, proliferation, migration, and survival necessary for fetal growth"[279] "stress induced neuroplasticity associated with altered HPA function is mediated by functional interactions between glucocorticoids and brain-derived neurotrophic factor (*BDNF*)"[290]		
Tissue	**Site**	**Exposure**	**Outcome**	**Sample**	**Results (paraphrased from sources as indicated)**
cord blood, placental tissue, and maternal venous blood	67 CpGs	chronic stress and war trauma	-	24 mother-baby dyads, Dem Rep of the Congo	maternal experiences of war trauma and chronic stress were significantly associated with *BDNF* methylation in all 3 tissues; results varied by CpG; for placental tissue, cg16257091, cg10635145, cg26840770, cg10558494, cg15313332, cg25962210, cg27193031, and cg27193031 were associated with war trauma, and cg26949694, cg25962210, and cg09492354 were associated with chronic stress[279]
blood		neighborhood socioeconomic disadvantage	-	1226 US adults aged 55-94	"for neighborhood socioeconomic disadvantage and neighborhood social environment, [there was]… at least one methylation site in the top 5% of EWAS results"[304]
blood		Everyday Discrimination Scale (EDS)	-	147 Latina women during preg and post-partum	"Significant negative associations were … identified at CpG sites 6 and 7 of the *BDNF* promoter (RR = 0.86, 0.92, p = 0.004, 0.004, respectively)."[290]
blood	exon VI	maternal care subscale of the Parental Bonding Instrument (PBI) (low vs high)	-	89 Swiss adults	"greater DNA methylation in the low versus high maternal care group, in the *BDNF* target sequence […; p=0.035]"[303]
Also of interest (very unusual to have any data on stillbirth): "[in this study of] *BDNF* expression in human cerebellar cortex of … 45 cases, aged between 25 gestational weeks and 6 postnatal months, including 29 victims of sudden fetal and infant death and 16 age-matched subjects who died of known causes (Controls).. [there was] in sudden death groups compared with Controls, a significantly higher incidence of defective *BDNF* expression in granule layers of the cerebellar cortex, which was particularly evident in the posterior lobule, a region that participates in respiratory control. These results were related to maternal smoking, allowing to speculate that nicotine, in addition to the well-known damages, can exert adverse effects during cerebellar cortex development, in particular in hindering the *BDNF* expression in the posterior lobule. This implies modifications of synaptic transmission in the respiratory circuits, with obvious deleterious consequences on survival"[424]					

FKBP5

CpGs	Location	Placental expression	Functions (paraphrased from sources as indicated)		
53 interrogated by 850k microarray	6p21.31; 13 exons	Low to medium [Genecards]	▪ **encodes glucocorticoid receptor (GR) co-chaperone protein (*FKBP51*)** ▪ "… undergoes rapid induction when cortisol activates GRs. *FKBP51* is thought to interrupt the feedback loop by binding to GRs, reducing affinity to cortisol and impeding GR translocation to the nucleus"[291]		
Tissue	**Site**	**Exposure**	**Outcome**	**Sample**	**Results (paraphrased from sources as indicated)**
placenta, cord, maternal venous		chronic stress and war trauma	birthweight	24 mother-baby dyads in Dem Rep of the Congo	"War Trauma-methylation associations were also observed at … *FKBP5* cg03546163 (surviving FDR correction)."[289]
placenta		Prenatal Distress Questionnaire and Perceived Stress Scale	fetal movement and heart rate ("coupling")	61 pregnant women (CUMC)	"higher Perceived Stress Scale score was consistently associated with greater DNA methylation (r=0.27–0.41; all p values <0.05); …birth weight corrected for gestational age… was inversely associated with *FKBP5* DNA methylation (block B) (r=−0.27, p<0.05); [mediation] Perceived Stress Scale was associated with greater DNA methylation (β=0.59, p<0.0001), which in turn was associated with lower fetal coupling (β=−0.47, p<0.01). This indirect effect was statistically significant (β=−0.27, p<0.05)."[281]
blood		neighborhood socioeconomic disadvantage	-	1226 US adults aged 55-94	"worse social environment was associated with increased methylation in shore/shelf sites;… for neighborhood socioeconomic disadvantage and neighborhood social environment, methylation sites in *FKBP5* …all had at least one methylation site in the top 5% of EWAS results"[304]
blood		child and adult SES and social mobility based on education	-	1,231 US adults aged 55-94	"low childhood SES was associated with increased DNAm [DNA methylation] in shore/ shelf sites (P = 0.03, q = 0.13) but was not associated in other site types"; also significant association with social mobility[305]
blood		Everyday Discrimination Scale (EDS)	-	147 Latina women during preg and post-partum	"significant negative association at CpG site 1 of *FKBP5* was identified (… p < 0.001)"[290]
maternal and infant saliva	Intron 7	adverse childhood experiences (Childhood Trauma Questionnaire (CTQ))	-	114 mothers and 107 infants in the USA	"in mothers carrying the stress sensitive T-allele (CT and TT genotypes), maternal *FKBP5* methylation negatively correlated with threat-based ACEs… In infants homozygous for the C allele (CC genotype), infant *FKBP5* methylation positively correlated with maternal threat-based ACEs [adverse childhood experiences]"[291]

HSD11B2

CpGs	Location	Placental expression	Functions (paraphrased from sources as indicated)		
23 interrogated by 850k microarray	16q22.1; 5 exons	Highly expressed in at least 1 cell type in the placenta [Genecards]	▪ "Placental *HSD11B2* is responsible for converting cortisol into inactive cortisone, thereby protecting the developing fetus from overexposure to glucocorticoids during development. However, this protective mechanism has limits. If *NR3C1* is dysregulated potentially from significant prenatal stressors, the protective effect of placental *HSD11B2* may be diminished, thereby allowing elevated levels of glucocorticoids into fetal circulation"[292] [from a study investigating interaction between methylation status of these 2 genes] ▪ "a key gene involved in glucocorticoid metabolism, which in turn seems to be related to fetal growth impairment"[266]		
Tissue	**CpG**	**Exposure**	**Outcome**	**Sample**	**Results (paraphrased from sources as indicated)**
placenta	4 CpGs in promoter region	prenatal socioeconomic adversity: maternal education, poverty, dwelling crowding, tobacco use and cumulative risk	-	444 healthy full-term newborns	"infants whose mothers experienced the greatest levels of socioeconomic adversity during pregnancy had the lowest extent of placental *HSD11B2* methylation, particularly for males. Associations were maintained for maternal education when adjusting for confounders ($p<0.05$)"[263]
placenta	4 CpGs in promoter region	-	birthweight, GA, ponderal index, length, IUGR	185 newborns	"Controlling for confounders, *HSD11B2* methylation extent is greatest in infants with the lowest birthweights ($P = 0.04$)… Moderate, statistically significant negative, correlations were observed between infant birthweight, and ponderal index (ratio of weight for length) and *HSD11B2* methylation…IUGR infants demonstrated a significantly greater extent of *HSD11B2* methylation ($P =0.007$)"[265]
placenta	four CpGs	depression or anxiety during pregnancy	NICU Network Neurobehavioral Scale (NNNS)	482 dyads from Rhode Island	"infants whose mothers reported anxiety during pregnancy and showed greater methylation of placental 11β-HSD-2 cpG4 were more hypotonic compared with infants of mothers who did not report anxiety during pregnancy"[306]
placenta	promoter	-	IUGR, birthweight, ponderal index	44 newborns in China	"methylation levels of all studied CpG sites were significantly higher in IUGR newborns than those in controls. Further, methylation levels of the first and the third CpG sites were inversely associated with measures of fetal growth (birth weight and ponderal index)"[266]
placenta	promoter region (3 CpGs)	-	infant neurobehavior (NICU Network Neurobehavioral Scales)	372 infants in Rhode Island	"Those with low *NR3C1* methylation but high *HSD11B2* methylation had lower excitability scores; those with high *NR3C1* methylation but low *HSD11B2* methylation had more asymmetrical reflexes; those with high DNA methylation across the entire pathway had higher habituation scores"[292]
placenta		Prenatal Distress Questionnaire and Perceived Stress Scale	fetal movement and heart rate ("coupling")	61 pregnant women (CUMC)	"higher Perceived Stress Scale score was consistently associated with greater DNA methylation ($r=0.27–0.41$; all p values <0.05);… Greater DNA methylation of *HSD11B2* was associated with less coupling ($r=−0.40$, $p<0.01$), [mediation] Perceived Stress Scale was associated with greater DNA methylation ($β=0.47$, $p<0.001$), which in turn was associated with lower fetal coupling ($β= −0.51$, $p<0.001$). This indirect effect (Perceived Stress Scale to fetal coupling through DNA methylation) was statistically significant ($β=−0.24$, $p<0.01$)"[281]

IGF2

CpGs	Location	Placental expression	Functions (paraphrased from sources as indicated)
47 interrogated by 850k microarray	11p15.5; 9 exons	Highly expressed in at least 1 cell type in the placenta [Genecards]	▪ "The insulin growth factor (IGF) system includes *IGF1* and *IGF2* as well as several other genes related to IGF-binding proteins. Though they are each expressed in various parts of the body, *IGF1* and *IGF2* are also both synthesized by the placenta, where they are involved in the regulation of fetal, placental and neonatal growth"[287] ▪ "implicated in fetal growth, imprinting syndromes, Wilms Tumour, obesity, metabolic syndrome"[294] ▪ "Reciprocally imprinted genes; paternally expressed *IGF2* encodes a member of the insulin family of polypeptide growth factors, which are involved in growth and development; maternally expressed H19 encodes a non-coding RNA, and functions as a tumor suppressor. Imprinting status has been correlated with various environmental exposures e.g. bisphenol A and smoking"[282] ▪ "Normally, *H19* DMR is methylated on the paternal allele preventing the binding of the zinc finger protein CTCF, which in turn allows the access of the *IGF2* promoter to the enhancers located downstream of *H19*, and consequently, paternal *IGF2* is expressed. On the other hand, in the maternal allele this CTCF-binding site is unmethylated, which allows the binding of CTCF and the interaction of the *H19* promoter to the enhancers. In this case, the *IGF2* is silenced and the H19 is expressed… deletion of the active copies of … the genes here studied, was shown to result in a noticeable placental phenotype, with most deletions affecting the size of the placenta"[269] ▪ "involved in specific gene networks that control fetal growth and development[288]

Tissue	Site	Exposure	Outcome	Sample	Results (paraphrased from sources as indicated)
maternal venous, cord blood and placental		war trauma and chronic stress	birthweight	24 mother-baby dyads in Dem Rep of the Congo	"strong association was found between newborn birth weight and *IGF2* PC2 methylation in mother's blood (P= 0.0027); … war and rape stress associated with *IGF2* methylation in maternal blood"[287]
placenta	Imprinting control region (ICR)	Perceived stress scale (PSS-14) (during past month), State-trait anxiety inventory (STAI), Life Experience Interview (measured the occurrence of stressful events; only for relationships and health)	-	50 NYC mothers	"both partner- and health-related stress life events were associated with ICR hypermethylation"[282]
placental and fetal tissue	two promoter regions, P0 and P3	-	2nd trimester fetal loss	35 2nd trimester losses (16 due to infection, 19 idiopathic)	"did not observe significant changes, although an hypomethylated state was noted in both promoters (P3 mean methylation percentage 3,9% in idiopathic SA [spontaneous abortions] vs 7,6% in controls; p > 0,05)"[269]
cord blood	4 CpGs	-	placental size, birthweight, neonatal treatment	1,236 mothers and 1,073 newborns in Scotland	"Placental size was related to … *IGF2* (p<0.001) methylation… Birth weight was related to … *IGF2* methylation but only at p= 0.052"[294]
cord blood		maternal depressed mood (Edinburgh Depression Scale; EDS), pregnancy-related anxiety questionnaire (PRAQ)	-	80 Belgian dyads	"We found a … (CpG)-specific association of PRAQ subscales with *IGF2* DMR0 (CpG5, P<0.0001)… *IGF2*AS was associated with maternal EDS scores (CpG33, P=0.0003)" "[288]

NR3C1

CpGs	Location	Placental expression	Functions (paraphrased from sources as indicated)		
89 interrogated by 850k microarray	5q31.3; 16 exons	Highly expressed in most cell types in the placenta [Genecards]	▪ **encodes glucocorticoid receptor** ▪ *"NR3C1* is the GC receptor and is involved in cell proliferation and differentiation and specifically implicated in newborn birth weight, thus providing a biological mechanism by which *NR3C1* expression may influence birth weight"[295] ▪ "… exon 1F hypermethylation in relation to … [early life adversity] has been demonstrated in peripheral tissues, including cord blood, white blood cells and whole blood … and would potentially result in dysregulation of HPA axis negative feedback were it occurring in the brain"[308] ▪ "Placental *HSD11B2* is responsible for converting cortisol into inactive cortisone, thereby protecting the developing fetus from overexposure to glucocorticoids during development. However, this protective mechanism has limits. If *NR3C1* is dysregulated potentially from significant prenatal stressors, the protective effect of placental *HSD11B2* may be diminished, thereby allowing elevated levels of glucocorticoids into fetal circulation"[292] [from a study investigating interaction between methylation status of these 2 genes]		
Tissue	**Site**	**Exposure**	**Outcome**	**Sample**	**Results (paraphrased from sources as indicated)**
placenta	exon 1F, 13 CpGs	-	infant neurobehavior (NICU Network Neurobehavioral Scales)	372 infants in Rhode Island	"Those with low *NR3C1* methylation but high *HSD11B2* methylation had lower excitability scores; those with high *NR3C1* methylation but low *HSD11B2* methylation had more asymmetrical reflexes; those with high DNA methylation across the entire pathway had higher habituation scores"[292]
placenta	promoter 1F region	-	birthweight	480 full-term placentas in Rhode Island	"significant association ($p < 0.0001$) between differential methylation of the GR gene and large for gestational age (LGA) status."[311]
placenta		Prenatal Distress Questionnaire and Perceived Stress Scale	fetal movement and heart rate ("coupling")	61 pregnant women (CUMC)	"higher Perceived Stress Scale score was consistently associated with greater DNA methylation (r=0.27–0.41; all p values <0.05)"[281]
placenta	13 CpGs in the exon 1F promoter region	depression or anxiety during pregnancy	NICU Network Neurobehavioral Scale (NNNS)	482 dyads from Rhode Island	"infants whose mothers reported depression during pregnancy and showed greater methylation of placental *NR3C1* cpG2 had poorer self-regulation, more hypotonia, and more lethargy than infants whose mothers did not report depression"[306]
placenta, cord, maternal venous	cg15910486, cg18019515, and cg27122725	chronic stress and war trauma	birthweight	24 mother-baby dyads in Dem Rep of the Congo	"Chronic Stress predicted methylation in … *NR3C1* and explained 16–25% of the variance, … War Trauma predicted methylation … (variance explained 13–35%) …reduced methylation at *NR3C1* cg15910486, cg18019515, and cg27122725 was significantly associated with War Trauma after FDR correction;.. methylation…predicted BW…*NR3C1* cg15910486, associated with Chronic Stress and War Trauma in placenta and located at 7 TFBs including the consensus NGFI-A binding site, *NR3C1* cg18019515, associated with War Trauma in placenta and located at 6 known TFBs, *NR3C1* cg24026230, associated with Chronic Stress (not FDR-corrected) in cord blood and situated at a POLR2A… methylation at these four sites [also in CRH] accounted for 55% of the variance in BW [birthweight]"[289]
varied (cord, placenta, buccal, saliva, whole blood)	5 analyzed CpGs (35 to 39) at the promoter of exon 1F	maternal chronic psychosocial stress (during pregnancy) (varied)	-	977 subjects across 7 studies (meta-analysis)	"significant correlation between offspring's methylation and prenatal stress (r = 0.14, 95% CI: 0.05–0.23, pr =0.002…)[309]

whole blood	exon 1F	Childhood Trauma Questionnaire (CTQ) covering abuse and neglect	-	67 cases and controls (depressed and not)	"significant positive association between the severity of emotional abuse [not other types] experienced during childhood and the degree of DNA methylation at *NR3C1* exon 1F CG37 (r=0.53, p=0.01) and CG38 (r=0.43, p=0.04) … This finding was only present in depressed individuals who reported ELA [early life adversity] and not in the overall sample."[308]
blood, saliva	1F exon	early life stress (ELS)	-	361 individuals from 4 studies (meta-analysis)	"epigenomic modulation associated with child ELS, hypermethylation was observed, CES [combined or common effect size] = 23.2%, 95%CI, 8.00–38.48" (Quantitative Evidence Synthesis, QES, of 4 studies)[310]
cord blood mononuclear cells	CpG-rich sequences for the promoter regions B, D and F	State Trait Anxiety Inventory (STAI), Pregnancy Related Anxiety Questionnaire (PRAQ), Maternal Fetal Attachment Scale (MFAS) at each trimester	-	83 women and babies in Belgium	"In a multivariable model the proportion of variance in methylation state of F9 explained (PVE) by pregnancy related anxiety was 7.8% (p = 0.023) during T1 … Different CpG-units located at the nerve growth factor inducible protein A (NGFI-A) binding sites of 1F were associated with maternal anxiety"[262]
cord blood mononuclear cells	47 CpGs including 1F exon	Perceived Stress Scale (PSS)	-	480 mother-baby dyads from Australia	"PSS scores positively correlated with methylation levels at CpG 1.2 (r = .11, p= .02) and CpG 3.4.5 (r = .12, p = .01…) [but] none of these associations remained significant after taking into account the multiple comparisons and the Bonferroni corrected p value threshold of .00079"[307]
maternal venous blood and umbilical cord	39 CpGs in upstream promoter	material deprivation intended to reflect availability of financial resources, mundane stressors to reflect daily psychosocial stress, and war stress	birthweight	25 mother-newborn dyads in Dem Rep of the Congo	"[there was] correlation between war stress and newborn methylation (when analyzed as the first principal component, i.e., PC1; … p = 0.0032). Furthermore, newborn methylation-PC1 is strongly correlated with newborn birth weight (…p = 0.024)… material deprivation and mundane stress are also correlated with newborn methylation-PC1… Cord methylation (PC1 of 39 CpG sites in the promoter region) is negatively associated with birthweight.[295] NOTE: LGA is a risk factor for stillbirth.[425 426] A possible mechanism is a relatively small placenta for size.[426]
blood		Everyday Discrimination Scale (EDS)	-	147 Latina women during preg and post-partum	"significant negative associations between EDS and methylation at CpG sites 1 and 2 of *NR3C1* (RR = 0.85, 0.84 and p = 0.008, 0.004, respectively)."[290]
blood		neighborhood socioeconomic disadvantage	-	1226 US adults aged 55-94	"for neighborhood socioeconomic disadvantage and neighborhood social environment, methylation sites … had at least one methylation site in the top 5% of EWAS results"[304]

Also of interest:

- Placental methylation of *NR3C1* affects infant neurobehavior (promoter region).[427] Similar results found here: [300]. Former study found greater mean methylation associated with reduced expression of *NR3C1* mRNA
- All the above: 13 CpGs in exon 1F of the promoter region
- Lower buccal methylation of CpG1 (promoter region) for infants in the high-risk vs low-risk group of preterm infants;[428] infants with high-risk vs low-risk neurobehavioral profile showed more methylation at CpG3[429]

Abbreviations: BW, birthweight; CUMC, Columbia University Medical Center; Dem Rep of the Congo, Democratic Republic of the Congo; DMR, differentially methylated region; EWAS, epigenome-wide association study; FDR, false discovery rate; GA, gestational age; GC, glucocorticoid; HPA, hypothalamus-pituitary-adrenal axis; ICR, imprinting control region; IUGR, intrauterine growth restriction; LGA, large for gestational age; NICU, neonatal intensive care unit; PC1 and PC2, principal component 1 and 2; preg, pregnant; RR, relative risk; SES, socioeconomic status; TFB, transcription factor binding.

Table A50: Characteristics of 1,191 CpGs on the five candidate genes: *BDNF, FKBP5, HSD11B2, IGF2, NR3C1*

		BDNF	***FKBP5***	***HSD11B2***	***IGF2***	***NR3C1***	***Total***
CpGs in promoters/ enhancers	Total # promoters/enhancers from Genecards	90	65	77	34	257	523
	Of which, identified by both ENCODE and Ensembl	31	23	40	21	79	194
	# CpGs in these promoters/enhancers and interrogated on the microarray	119	141	327	330	213	1130
CpGs of interest that are interrogated by the microarray	# CpGs only in gene body	28	21	3	11	24	87
	# CpGs only in enhancer	22	8	43	66	129	268
	# CpGs only in promoter/enhancer	44	105	270	164	23	606
	# CpGs in both gene body and enhancer [a]	4	3	0	0	16	23
	# CpGs in both gene body and promoter/enhancer [a]	49	25	14	100	45	233
	Total # CpGs in gene body	81	49	17	111	85	343
	Total # CpGs in enhancer or promoter/enhancer	119	141	327	330	213	1130
	Total # CpGs of interest	147	162	330	341	237	1217
Of these, CpGs for which beta values were available	# CpGs in gene body	80	49	17	111	85	342
	# CpGs in enhancer	23	11	42	64	143	283
	# CpGs in promoter/enhancer	93	124	277	259	68	821
	Total # CpGs of interest	144	156	322	334	235	1191

[a] *Enhancer and promoter/enhancer regions can be on gene bodies or upstream/downstream of gene bodies; hence a single CpG may be noted as being on a gene body as well as one of these other regions.*

Table A51: Odds ratios (95% CIs) relating stressors (SLE and Disadvantage) and stillbirth in the study sample (n=183) and SCRN (n=1,479): Continuous versions of exposures

	Study		SCRN	
	OR (95% CI)	**aOR [a] (95% CI)**	**OR (95% CI)**	**aOR [a] (95% CI)**
Disadvantage	1.54 (1.07, 2.27)	1.80 (1.18, 2.74)	1.34 (1.08, 1.67)	1.48 (1.17, 1.88)
SLE	1.15 (0.97, 1.36)	1.11 (0.92, 1.33)	1.08 (0.98, 1.20)	1.03 (0.93, 1.15)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; ref, reference level; SCRN, Stillbirth Collaborative Research Network; SLE, Significant Life Events.
[a] Adjusted for maternal age, site, and race. SLE aORs also adjusted for Disadvantage (measured continuously).

Table A52: Sensitivity analyses for associations between maternal stressors, measured by SLE and Disadvantage, and stillbirth in the study sample

	Primary analysis [b] (n=183)	Sensitivity analysis A [c] (n=180)	Sensitivity analysis B [d] (n=183)
	aOR (95% CI) [a]	aOR (95% CI) [a]	aOR (95% CI) [a]
Disadvantage			
continuous	1.80 (1.18, 2.74)	1.89 (1.23, 2.91)	2.07 (1.23, 3.50)
categorical			
0 items	ref	ref	ref
1 item	1.65 (0.76, 3.56)	1.78 (0.80, 3.96)	2.16 (1.00, 4.67)
2+ items	4.53 (1.58, 12.93)	5.04 (1.73, 14.66)	7.16 (1.57, 32.64)
SLE			
continuous	1.11 (0.92, 1.33)	1.13 (0.94, 1.36)	
categorical			
0 events	ref	ref	
1 event	1.15 (0.41, 3.17)	1.18 (0.41, 3.42)	
2 events	1.71 (0.61, 4.83)	1.95 (0.67, 5.69)	
3 events	1.20 (0.36, 4.05)	1.35 (0.39, 4.65)	
4+ events	1.54 (0.55, 4.28)	1.71 (0.60, 4.88)	

Abbreviations: aOR, odds ratio; CI, confidence interval; OR, odds ratio; ref, reference level; SCRN, Stillbirth Collaborative Research Network; SLE, Significant Life Events.

[a] Adjusted for maternal age, site, and race. SLE aORs also adjusted for Disadvantage (measured continuously).

[b] Primary analysis replicated from Table 9 for convenience.

[c] Sensitivity analysis A: tested associations between stress and stillbirth in a subset of the study sample (n=180) excluding three stillbirths: two outliers and one sample that had received multiple quality control flags during bisulfite conversion (see Appendix B).

[d] Sensitivity analysis B: tested associations between Disadvantage and stillbirth using a modified version of Disadvantage that excludes partnership status.

Table A53: Differentially methylated CpGs with respect to stillbirth or Disadvantage: n=35 of 1,191 CpGs examined, ordered by genomic location

Probe					Promoter [e]		Mean β [f]		Stillbirth [g]		Index of Disadvantage [g]								
ID [m]	Chr	Gene	Start [a,b]	Reg [c,d]	ID [d]	Location [a]	SB	LB	OR (95% CI)	P [l]	1v0 (95% CI) [h]	β [k]	P [l]	2+v0 (95% CI) [i]	β [k]	P [l]	ea item (95% CI) [j]	β [k]	P [l]
cg17140497	5	*NR3C1*	143,183,611	E	GH05J143182	143181202-143184399	68.4	70.3	1.15 (0.91, 1.47)	0.238	-0.01 (-0.06, 0.04)	0.11	0.732	-0.03 (-0.09, 0.04)	0.35	0.430	-0.01 (-0.03, 0.02)	0.12	0.502
cg04090712	5	*NR3C1*	143,244,226	E	GH05J143241	143241504-143246872	23.1	20.2	1.38 (1.01, 1.91)	0.050	0.02 (-0.02, 0.07)	0.32	0.311	-0.01 (-0.08, 0.05)	0.15	0.724	0.00 (-0.03, 0.02)	0.02	0.893
cg15115787	5	*NR3C1*	143,351,135	B	NA	NA-NA	60.5	62.2	1.22 (1, 1.51)	0.062	-0.04 (-0.09, 0.01)	0.32	0.144	0.01 (-0.06, 0.07)	0.05	0.856	0.00 (-0.03, 0.03)	0.01	0.931
cg25026500	6	*FKBP5*	34,888,109	P/E	GH06J034886	34886400-34892632	7.5	7.4	1.67 (1.08, 2.69)	0.027	0.04 (-0.03, 0.12)	0.23	0.270	0.05 (-0.05, 0.16)	0.28	0.304	0.03 (-0.01, 0.07)	0.17	0.119
cg00065598	6	*FKBP5*	35,342,218	P/E	GH06J035341	35341664-35345401	4.7	4.1	1.99 (1.23, 3.38)	0.007	-0.01 (-0.14, 0.11)	0.08	0.818	-0.02 (-0.19, 0.15)	0.11	0.812	-0.02 (-0.08, 0.05)	0.09	0.612
cg25324046	6	*FKBP5*	35,921,281	P/E	GH06J035918	35918000-35923105	7.5	7.1	1.67 (1.11, 2.68)	0.022	0.00 (-0.09, 0.08)	0.05	0.912	0.05 (-0.06, 0.17)	0.51	0.367	0.01 (-0.04, 0.05)	0.10	0.670
cg05096964	11	*IGF2*	1,694,061	E	GH11J001690	1689601-1694740	10.1	9.3	1.58 (1.11, 2.4)	0.021	-0.04 (-0.12, 0.04)	0.35	0.325	0.09 (-0.01, 0.20)	0.86	0.084	0.02 (-0.02, 0.07)	0.23	0.259
cg12283393	11	*IGF2*	1,853,214	P/E	GH11J001849	1849656-1855952	78.1	82.5	0.81 (0.68, 0.97)	0.021	0.03 (-0.09, 0.14)	0.12	0.643	-0.15 (-0.31, 0.00)	0.67	0.047	-0.05 (-0.11, 0.01)	0.19	0.128
cg03776775	11	*IGF2*	1,950,271	P/E	GH11J001947	1946001-1959440	73.6	72.6	1.53 (1.22, 1.99)	0.001	0.05 (-0.06, 0.16)	0.90	0.340	0.03 (-0.12, 0.17)	0.42	0.739	0.03 (-0.03, 0.09)	0.53	0.286
cg19150916	11	*IGF2*	1,952,485	P/E	"	"	71.4	70.4	1.34 (1.05, 1.75)	0.024	0.03 (-0.02, 0.08)	0.47	0.262	0.01 (-0.05, 0.08)	0.24	0.669	0.01 (-0.01, 0.04)	0.23	0.298
cg14681632	11	*IGF2*	1,953,049	P/E	"	"	75.6	74.7	1.42 (1.15, 1.81)	0.002	0.05 (0.00, 0.11)	0.91	0.067	0.03 (-0.05, 0.11)	0.52	0.435	0.03 (0.00, 0.06)	0.45	0.090
cg10113191	11	*IGF2*	1,953,101	P/E	"	"	61.7	61.2	1.48 (1.14, 1.96)	0.005	0.01 (-0.03, 0.05)	0.09	0.798	0.01 (-0.04, 0.07)	0.25	0.592	0.01 (-0.01, 0.04)	0.25	0.164
cg19290938	11	*IGF2*	1,967,527	E	GH11J001962	1962371-1972699	31.0	27.2	1.24 (1.06, 1.47)	0.009	0.00 (-0.07, 0.08)	0.02	0.916	0.03 (-0.08, 0.13)	0.14	0.624	0.01 (-0.03, 0.05)	0.06	0.603
cg24465592	11	*IGF2*	1,967,955	E	"	"	26.4	21.8	1.26 (1.03, 1.56)	0.030	-0.04 (-0.12, 0.03)	0.31	0.235	-0.05 (-0.14, 0.05)	0.32	0.367	-0.03 (-0.07, 0.01)	0.20	0.146
cg19425295	11	*IGF2*	1,968,002	E	"	"	22.2	17.2	1.4 (1.14, 1.75)	0.002	0.01 (-0.09, 0.10)	0.05	0.878	0.03 (-0.09, 0.16)	0.20	0.607	0.00 (-0.05, 0.05)	0.02	0.921
cg05894719	11	*IGF2*	1,968,668	E	"	"	22.8	18.9	1.25 (1.07, 1.49)	0.007	0.03 (-0.07, 0.13)	0.39	0.539	0.08 (-0.05, 0.21)	1.02	0.222	0.02 (-0.03, 0.07)	0.21	0.518
cg03982897	11	*IGF2*	1,968,877	E	"	"	14.1	11.4	1.76 (1.26, 2.58)	0.002	-0.03 (-0.12, 0.05)	0.52	0.458	0.08 (-0.03, 0.20)	1.33	0.165	0.02 (-0.03, 0.06)	0.29	0.446
cg16574793	11	*IGF2*	2,001,093	P/E	GH11J001985	1985257-2003509	61.4	58.8	1.17 (1.08, 1.28)	0.000	0.02 (-0.12, 0.17)	0.19	0.744	0.09 (-0.10, 0.28)	0.69	0.370	0.03 (-0.04, 0.11)	0.24	0.426
cg02097792	11	*IGF2*	2,036,815	E	GH11J002034	2034147-2040284	27.3	26.3	1.34 (1.11, 1.67)	0.005	0.05 (-0.02, 0.12)	0.63	0.134	0.10 (0.00, 0.19)	1.16	0.044	0.04 (0.01, 0.08)	0.51	0.024
cg01667319	11	*IGF2*	2,139,897	P/E, B	GH11J002131	2131551-2152660	12.7	11.8	1.24 (1.09, 1.43)	0.002	0.02 (-0.14, 0.19)	0.03	0.779	0.01 (-0.21, 0.23)	0.01	0.935	-0.01 (-0.10, 0.07)	0.02	0.781
cg10037494	11	*IGF2*	2,139,904	P/E, B	"	"	6.7	6.1	1.2 (1.07, 1.36)	0.002	0.07 (-0.24, 0.37)	0.02	0.657	0.06 (-0.35, 0.47)	0.01	0.775	0.00 (-0.16, 0.16)	0.00	0.985
cg25163476	11	*IGF2*	2,140,355	P/E, B	"	"	13.8	12.0	1.13 (1.04, 1.23)	0.003	0.10 (-0.13, 0.34)	0.90	0.392	0.03 (-0.29, 0.35)	0.27	0.846	0.00 (-0.13, 0.12)	0.00	0.993
cg08362738	11	*BDNF*	27,701,088	P/E, B	GH11J027697	27696216-27702539	3.9	3.5	2.05 (1.09, 3.99)	0.029	0.03 (-0.08, 0.13)	0.28	0.618	0.14 (0.00, 0.29)	1.53	0.048	0.05 (0.00, 0.11)	0.60	0.057
cg04672351	11	*BDNF*	27,701,341	P/E, B	"	"	8.0	7.6	2.03 (1.28, 3.44)	0.005	-0.04 (-0.11, 0.03)	0.31	0.247	0.09 (0.00, 0.18)	0.70	0.058	0.02 (-0.01, 0.06)	0.18	0.233
cg27309677	11	*BDNF*	28,108,257	P/E	GH11J028105	28105533-28111801	6.5	6.1	1.49 (1.04, 2.23)	0.039	-0.03 (-0.13, 0.07)	0.16	0.593	0.02 (-0.12, 0.15)	0.11	0.789	0.00 (-0.05, 0.05)	0.00	0.990
cg19372491	11	*BDNF*	28,108,422	P/E	"	"	6.8	6.4	1.93 (1.29, 3.03)	0.002	-0.03 (-0.13, 0.06)	0.16	0.496	0.00 (-0.13, 0.13)	0.00	0.990	0.00 (-0.05, 0.06)	0.02	0.876
cg01087710	16	*HSD11B2*	67,110,271	P/E	GH16J067108	67108921-67111835	6.0	5.6	1.65 (1.14, 2.51)	0.012	-0.13 (-0.23, -0.02)	0.78	0.019	-0.03 (-0.18, 0.11)	0.20	0.655	-0.03 (-0.08, 0.03)	0.18	0.339
cg05477463	16	*HSD11B2*	67,184,151	P/E	GH16J067182	67182600-67188059	6.6	6.1	1.56 (1.1, 2.34)	0.022	-0.01 (-0.12, 0.09)	0.07	0.810	0.06 (-0.08, 0.20)	0.31	0.413	0.02 (-0.04, 0.07)	0.09	0.564
cg05413199	16	*HSD11B2*	67,396,550	P/E	GH16J067389	67389216-67400723	21.3	17.5	1.36 (1.07, 1.76)	0.015	-0.04 (-0.12, 0.03)	0.31	0.239	-0.02 (-0.12, 0.08)	0.13	0.706	-0.02 (-0.06, 0.02)	0.11	0.413
cg10434888	16	*HSD11B2*	67,481,109	P/E	GH16J067479	67479000-67484532	8.6	7.5	1.24 (1.07, 1.45)	0.005	-0.07 (-0.27, 0.12)	1.27	0.450	-0.01 (-0.27, 0.25)	0.21	0.927	-0.02 (-0.12, 0.08)	0.32	0.720
cg03498304	16	*HSD11B2*	67,842,237	P/E	GH16J067841	67841200-67848801	3.1	2.4	1.51 (1.11, 2.18)	0.014	-0.13 (-0.36, 0.10)	0.25	0.269	0.28 (-0.02, 0.59)	0.63	0.069	0.08 (-0.04, 0.20)	0.21	0.201
cg05632351	16	*HSD11B2*	67,847,657	P/E	"	"	5.0	4.4	1.67 (1.16, 2.53)	0.010	-0.17 (-0.32, -0.01)	1.50	0.035	-0.07 (-0.28, 0.14)	0.63	0.516	-0.06 (-0.14, 0.02)	0.58	0.145
cg19413291	16	*HSD11B2*	67,884,391	P/E	GH16J067880	67879801-67886800	79.8	78.9	1.29 (1.09, 1.54)	0.004	0.05 (-0.03, 0.13)	0.89	0.215	0.14 (0.03, 0.25)	2.36	0.014	0.06 (0.02, 0.10)	1.05	0.005
cg00511334	16	*HSD11B2*	67,884,936	P/E	"	"	41.5	38.8	1.28 (1.07, 1.55)	0.010	0.03 (-0.02, 0.09)	0.48	0.198	-0.03 (-0.10, 0.04)	0.38	0.459	0.00 (-0.03, 0.02)	0.04	0.838
cg21445230	16	*HSD11B2*	67,935,463	P/E	GH16J067934	67934255-67938278	13.7	11.9	1.29 (0.92, 1.82)	0.142	-0.02 (-0.09, 0.05)	0.31	0.630	0.03 (-0.07, 0.13)	0.56	0.515	0.01 (-0.03, 0.05)	0.17	0.602

Abbreviations: Chr, chromosome; CI, confidence interval; LB, livebirth; OR, odds ratio; Reg, region; SB, stillbirth.

[a] Build 38 used.

[b] Start is genomic location of first CpG base pair.

[c] P, E, B indicate whether CpG is in promoter or enhancer or on gene body, respectively.

[d] Region type and Promoter ID from GeneCards.

[e] Single promoter regions are highlighted in light grey.

[f] Mean β is the mean percent methylation for stillbirths (SB) and livebirths (LB).

[g] All associations adjusted for cell type (trophoblast, stromal, endothelial, nRBC, and syncytiotrophoblast), maternal age and race, site, and plate. Associations

*with stillbirth additionally adjusted for sex. ORs from logistic regression using β values * 100; interpretable as the adjusted odds ratio for stillbirth with a one-percentage point increase in methylation. Estimates of associations between methylation and Disadvantage from linear regression using M values.*

[h] *"1v0" is mean difference in M-values for 1 as compared to no items in the Index of Disadvantage.*

[i] *"2+v0" is mean difference in M-values for 2+ as compared to no items in the Index of Disadvantage.*

[j] *"ea item" is mean difference in M-values for every additional item in the Index of Disadvantage.*

[k] *β is mean difference in % methylation in β values for the respective estimate, using the method of Kruppa et al.*[321]

[l] *All p-values unadjusted.*

[m] *CpGs for which p<0.05 for both Disadvantage and stillbirth are highlighted in dark grey: cg12283393, cg02097792, cg08362738, cg01087710, cg05632351, and cg19413291. CpGs for which directions of association with respect to stillbirth and Disadvantage are the same are the four mediator candidates: cg12283393, cg02097792, cg08362738, and cg19413291.*

Table A54: Differentially methylated regions with respect to stillbirth or Disadvantage: n=6 from 1,191 CpGs examined

							Stillbirth [b]		Index of Disadvantage [b]								
ID	Chr	Gene	Start [c]	Length (bp)	mean β (SD) [a]	constituent CpGs	OR (95% CI)	P [h]	1v0 (95% CI) [d]	β [g]	P [h]	2+v0 (95% CI) [e]	β [g]	P [h]	ea item (95% CI) [f]	β [g]	P [h]
DMR_1_1	11	*IGF2*	1,989,186	48	21.1 (5.9)	cg24465592	1.43 (1.14, 1.85)	0.004	-0.021 (-0.096, 0.053)	0.001	0.573	-0.011 (-0.111, 0.089)	0.001	0.824	-0.017 (-0.056, 0.022)	0.001	0.386
						cg19425295											
DMR_1_2	11	*IGF2*	1,989,850	259	18.6 (4.6)	cg03982897	1.34 (1.07, 1.69)	0.012	0.020 (-0.062, 0.101)	0.003	0.636	0.071 (-0.038, 0.181)	0.010	0.200	0.016 (-0.027, 0.059)	0.002	0.458
						cg05894719											
						cg27617775											
DMR_1_3	11	*IGF2*	2,022,324	63	58.8 (4.7)	cg09452478	1.2 (1.09, 1.35)	0.001	0.018 (-0.087, 0.124)	0.002	0.733	0.046 (-0.096, 0.188)	0.006	0.523	0.018 (-0.038, 0.074)	0.002	0.523
						cg16574793											
DMR_1_4	11	*IGF2*	1,974,132	201	68.1 (3.7)	cg10113191	1.79 (1.32, 2.52)	<0.001	0.016 (-0.023, 0.055)	0.003	0.427	-0.004 (-0.057, 0.049)	0.001	0.875	0.009 (-0.012, 0.030)	0.002	0.403
						cg14681632											
						cg19273253											
						cg19837124											
						cg23266869											
DMR_1_5	11	*IGF2*	2,161,079	508	13.3 (2.7)	cg01667319	1.35 (1.14, 1.63)	0.001	0.000 (-0.121, 0.121)	0.000	0.997	-0.112 (-0.275, 0.050)	0.008	0.174	-0.059 (-0.123, 0.004)	0.004	0.066
						cg05859777											
						cg17434309											
						cg05452899											
						cg10037494											
						cg26517849											
						cg09694722											
						cg19371526											
						cg15393937											
						cg23905216											
						cg19443075											
						cg22287492											
						cg10659464											
						cg13756879											
						cg14188639											
						cg25163476											
DMR_1_6	11	*BDNF*	28,129,676	343	6.0 (1.2)	cg06544937	1.59 (1.06, 2.58)	0.037	-0.077 (-0.160, 0.006)	0.003	0.067	0.041 (-0.070, 0.152)	0.002	0.466	0.002 (-0.042, 0.046)	0.000	0.936
						cg19372491											
						cg14927277											
						cg21118186											
						cg20566942											
						cg21046078											
						cg23490773											
						cg08967200											
						cg14744160											
						cg16497921											
						cg27309677											

Abbreviations: bp, base pairs; Chr, chromosome; CI, confidence interval; DMR, differentially methylated region; OR, odds ratio; SD, standard deviation.

[a] Mean β is the mean percent methylation for the DMR.

*[b] All associations adjusted for cell type (trophoblast, stromal, endothelial, nRBC, and syncytiotrophoblast), maternal age and race, site, and plate. Associations with stillbirth additionally adjusted for sex. ORs from logistic regression using β values * 100; interpretable as the adjusted odds ratio for stillbirth with a one-percentage point increase in average methylation across all constituent CpGs in the DMR. Estimates of associations between methylation and Disadvantage from linear regression using M values.*

[c] *Start genomic locations are from Build 37 (DMRcate output).*
[d] *"1v0" is mean difference in M-values for 1 as compared to no items in the Index of Disadvantage.*
[e] *"2+v0" is mean difference in M-values for 2+ as compared to no items in the Index of Disadvantage.*
[f] *"ea item" is mean difference in M-values for every additional item in the Index of Disadvantage.*
[g] *β is mean difference in % methylation in beta values for the respective estimate, using the method of Kruppa et al.*[321]
[h] *All p-values unadjusted.*

Table A55: Pearson correlation coefficients for methylation beta values of constituent CpGs of n=6 DMRs

ID [a]																
1	cg24465592	cg24465592														
	cg19425295	0.94														
2	cg03982897	cg03982897	cg05894719													
	cg05894719	0.85														
	cg27617775	0.85	0.86													
3	cg09452478	cg09452478														
	cg16574793	0.76														
4	cg10113191	cg10113191	cg14681632	cg19273253	cg19837124											
	cg14681632	0.86														
	cg19273253	0.81	0.79													
	cg19837124	0.80	0.83	0.73												
	cg23266869	0.78	0.77	0.75	0.70											
5	cg01667319	cg01667319	cg05859777	cg17434309	cg05452899	cg10037494	cg26517849	cg09694722	cg19371526	cg15393937	cg23905216	cg19443075	cg22287492	cg10659464	cg13756879	cg14188639
	cg05859777	0.40														
	cg17434309	0.17	0.32													
	cg05452899	0.60	0.34	0.13												
	cg10037494	0.67	0.34	0.12	0.84											
	cg26517849	0.45	0.47	0.12	0.53	0.56										
	cg09694722	0.13	0.09	-0.06	0.07	-0.02	0.18									
	cg19371526	0.29	0.21	0.09	0.11	0.12	0.20	0.25								
	cg15393937	0.33	0.35	0.23	0.14	0.18	0.21	-0.01	0.40							
	cg23905216	0.34	0.37	0.23	0.12	0.14	0.19	0.01	0.32	0.84						
	cg19443075	0.29	0.33	0.24	0.20	0.21	0.25	0.00	0.31	0.80	0.70					
	cg22287492	0.21	0.24	0.29	0.08	0.10	0.15	-0.03	0.14	0.62	0.48	0.68				
	cg10659464	0.17	0.12	0.13	0.12	0.11	0.09	0.04	0.30	0.37	0.36	0.40	0.25			
	cg13756879	0.24	0.14	0.15	0.23	0.19	0.31	0.18	0.32	0.19	0.21	0.18	0.13	0.33		
	cg14188639	0.18	0.10	0.10	0.17	0.15	0.16	-0.01	0.02	0.22	0.16	0.16	0.11	0.03	0.03	
	cg25163476	0.27	0.28	0.18	0.19	0.20	0.19	0.07	0.16	0.38	0.33	0.39	0.28	0.17	0.10	0.12
6	cg06544937	cg06544937	cg19372491	cg14927277	cg21118186	cg20566942	cg21046078	cg23490773	cg08967200	cg14744160	cg16497921					
	cg19372491	0.09														
	cg14927277	-0.02	0.38													
	cg21118186	-0.12	0.36	0.50												
	cg20566942	0.04	0.24	0.36	0.62											
	cg21046078	-0.10	0.44	0.45	0.70	0.52										
	cg23490773	-0.10	0.32	0.43	0.81	0.66	0.65									
	cg08967200	-0.11	0.32	0.36	0.77	0.62	0.61	0.86								
	cg14744160	-0.11	0.39	0.42	0.80	0.60	0.67	0.87	0.89							
	cg16497921	-0.08	0.45	0.40	0.67	0.52	0.66	0.72	0.72	0.71						
	cg27309677	-0.11	0.35	0.51	0.75	0.60	0.67	0.77	0.75	0.77	0.70					

Abbreviation: DMR, differentially methylated region.
[a] ID 1 is DMR_1_1, 2 is DMR_1_2, etc.

Table A56: Pearson correlation for methylation beta values of the four mediator candidates

	cg12283393	cg02097792	cg08362738	cg19413291
cg12283393				
cg02097792	-0.31			
cg08362738	-0.26	0.16		
cg19413291	-0.23	0.16	-0.06	

Table A57: Results of assessing evidence for whether methylation of 4 CpGs mediates associations between Disadvantage and stillbirth: Average causal mediation effect (ACME) *p*-values and average proportions of the effect mediated (PME) in 63 stillbirths and 120 livebirths: Continuous version of exposure

			Mediation effect [a,c]			Mean methylation beta values, SD (# births)	
ID	**Chr**	**Gene**	**ACME *P* [b]**	**PME**	**PME *P* [b]**	**Stillbirths**	**Livebirths**
cg02097792	11	*IGF2*	0.012	21.2%	0.031	27.3, 2.7 (63)	26.2, 2.8 (120)
cg12283393	11	*IGF2*	0.093	12.3%	0.115	78.1, 7.5 (63)	82.6, 3.3 (120)
cg19413291	16	*HSD11B2*	0.051	23.9%	0.105	79.8, 2.8 (63)	78.8, 2.8 (120)
cg08362738	11	*BDNF*	0.112	13.7%	0.131	3.9, 0.8 (63)	3.5, 0.7 (120)

Abbreviations: ACME p, p-value for the average causal mediation effect; Chr, chromosome; CI, confidence interval; OR, odds ratio; PME p, p-value for the average proportion of the effect mediated; SD, standard deviation.
[a] Mediation models (one per CpG) used logistic regression and M values, and adjusted for site, maternal age, race, plate, cell type (trophoblast, stromal, endothelial, nRBC, and syncytiotrophoblast), and sex.
[b] p-values uncorrected.
[c] ACME and PME for continuous version of Disadvantage estimated from contrasting 1 vs 0 items in the Index. Estimates were produced for all other contrasts; for 2 vs 1 and 4 vs 3 contrasts, the results were similar to 1 vs 0; but for 3 vs 2 contrast, 0 cell counts for site=Emory produced an error so estimates were unavailable.

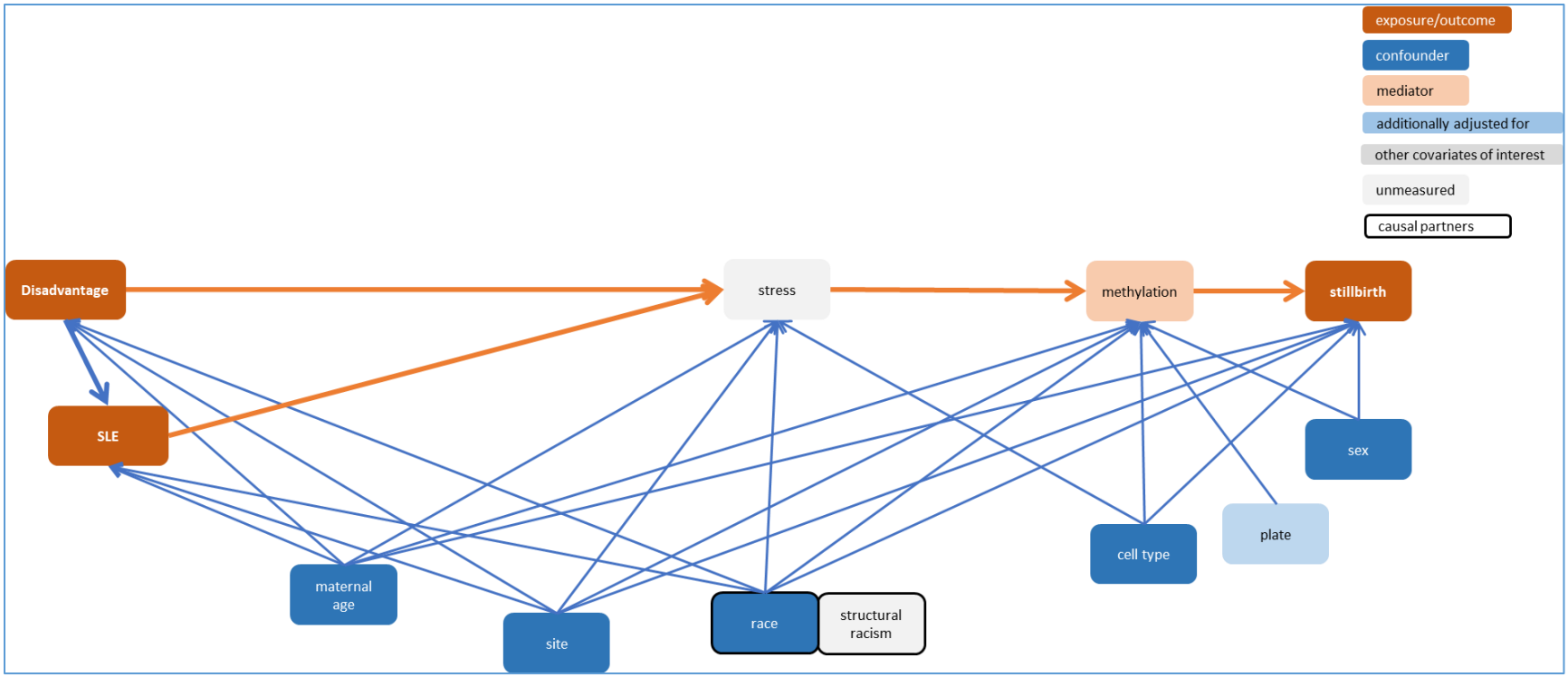


Figure A8: Theoretical diagram for associations between stressors and stillbirth

Abbreviations: SLE, Significant Life Events.

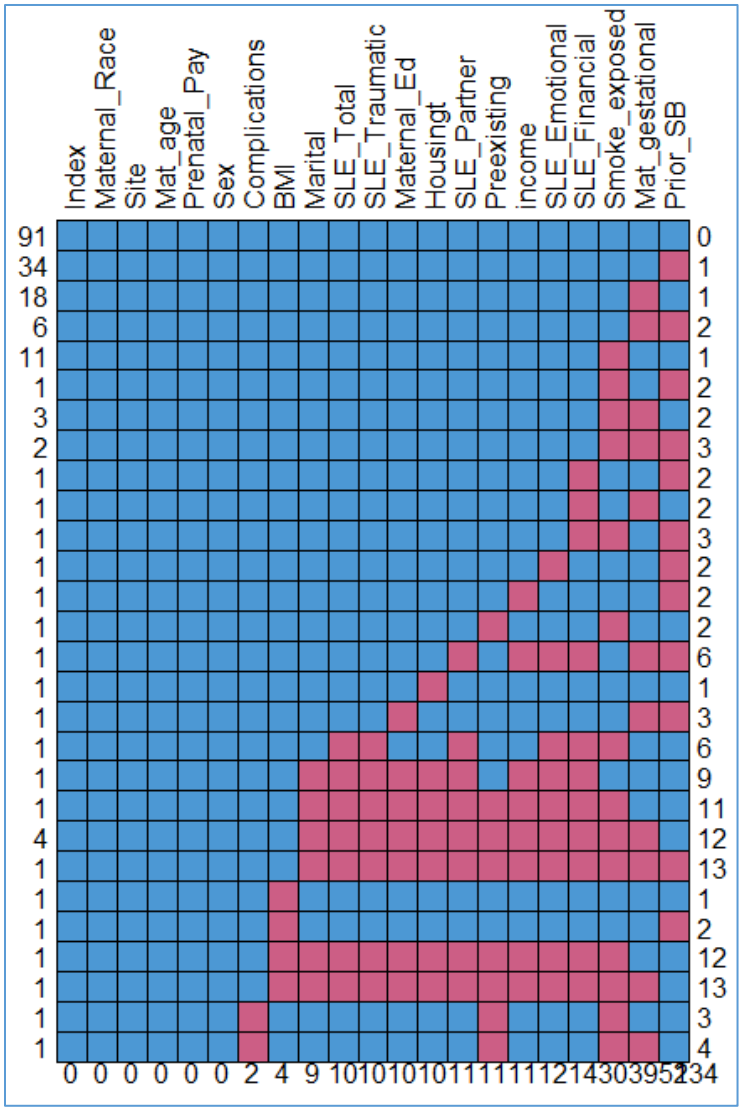


Figure A9: Missingness for 21 covariates in study sample (n=189)

Each row represents a unique missingness pattern. Red cells indicate that values are missing for this pattern (row) and covariate (column). Numbers in lefthand margin add up to 189 (total number of births in the study sample). There are 21 columns, one for each covariate whose missingness is represented in this table.
Two examples to help with interpretation of this table:
***top row**: lefthand number, 91, indicates that 91 of the 189 births had this missingness pattern; righthand number, 0, indicates that 0 of 21 covariates included in this table had missing values for this missingness pattern.*
***bottom row**: lefthand number, 1, indicates that one of 189 births had this missingness pattern; righthand number, 4, indicates that 4 of 21 covariates included in this table had missing values for this missingness pattern.*

Appendix B: Additional details of methods

Additional details of methods for Chapter 2

Abstract/title screening: *First phase*: In the first phase, two reviewers (SHL and EL) carried out double abstract/title screening of the 1,924 unique reports that were found through database searching. In this phase, the reviewers first piloted double-screening, and proceeded only after achieving 90% agreement. The inclusion criterion was:

- Report that includes stillbirth rates stratified by race/ethnicity from a cohort, case-control, cross-sectional, ecological or other study type (including both single studies and multiple studies reported through literature reviews).

Literature reviews with potentially relevant included studies were siphoned to our snowball review (see below), where we carried out title/abstract review of the potentially relevant included studies and then obtained full texts for any that passed this step of screening. In no case did we use study data reported within literature reviews. Exclusion criteria were:

- Non-human;
- Does not include pregnancy outcomes;
- Includes pregnancy outcomes but only live births;
- Only a discussion or overview, or otherwise does not report results of a study or studies;

- Only includes one racial/ethnic group (if only "Black" was included, the report was included in case there was further stratification into Hispanic and non-Hispanic Black).

For reports with no abstract, the title was generally used for screening, however on a few occasions the full text was briefly examined at this stage if there was any question about its possible relevance. To pilot this phase, the first 15 reports (going by author's name alphabetically) were screened. There was 80% agreement. The criteria were revised and clarified and the next 15 reports were screened, yielding 73% agreement. The criteria were further revised and piloted on a further 30 reports. With 90% agreement at this stage, screening of the remainder of the reports proceeded. All conflicts were then settled through discussion between the two reviewers. In the event of remaining disagreement, the report was included.

Second phase: The first screening yielded 934 included reports. To reduce this number further, a single reviewer (SHL) carried out a second title/abstract review with the following additional exclusion criteria:

- New exclusion criteria:
    - Abstracts only available. Rationale: limited room for authors to comment on racial disparities, a focus of this review.
    - Assisted reproductive technology (ART) focus. Rationale: to reduce number of reports for full text review; this was one of the few sizeable categories of report left that could be clearly identified and reasonably be excluded.
    - Data source: If data source was specified as National Center for Health Statistics (NCHS) birth certificate data, NCHS linked birth-infant death file, Pregnancy Risk Assessment Monitoring System (PRAMS) or natality file, unless fetal death files were specifically also included.

- Tightened or clarified criteria:
    - Any document that was not a study or review, including commentaries, editorials, news articles, overviews of diseases, and protocols;
    - Reports with the following outcomes were included, even if mentioned just in passing and not reported in the results section of abstract:
        - stillbirth, fetal/perinatal death, infant mortality (and abortion if it was unclear whether abortion meant elective)
        - pregnancy/birth/fetal/perinatal/neonatal outcomes
        - preterm birth/gestational age
        - low birthweight/SGA/IUGR/FGR/macrosomia

Third phase: The second screening yielded 671 included reports. To reduce this number further, a single reviewer (SHL) carried out a third title/abstract review with the following additional exclusion criteria:

- non-U.S. studies;
- literature reviews (these were saved separately for snowball review).

Full text review: Double full text review was carried out for 456 reports, including all 417 reports screened from phase 3 of title/abstract review as well as all 39 reports identified through snowball review. Full text review was piloted for ten reports; there was 40% agreement so another ten reports were piloted, with 90% agreement. Thereafter the remainder of the full text review was carried out, with the following process:

- Methods section:
    - Is it clear that only live births were included and/or stillbirth was excluded? Exclude.

- Results section:
    - Tables and figures: Is stillbirth rate presented and stratified by race/ethnicity? Include.
    - Results text: Is stillbirth rate stated and stratified by race/ethnicity? Include.
- If still uncertain, check whether there is a supplement/appendix (search for these terms: supple, annex, appendix):
    - If yes, check contents of same to see if there may be a table, figure or text that includes stillbirth rate presented and stratified by race/ethnicity.
    - If found, include.
- If still uncertain, search text for the following text strings: "stillb, live, fetal, misc"
    - If stillbirth rates are found and stratified by race/ethnicity, include.
    - Otherwise, exclude.
- Exclude if stillbirth rates are only presented as part of a composite outcome, or if unclear/unknown whether stillbirth data are presented (e.g., 'perinatal death' but not defined anywhere to clearly include stillbirth).
- "Stillbirth rate" above includes stillbirth ratios, rates, numbers, percents, or other quantities presented in text, tables or figures.

Exclusion criteria were:

- Live birth only. It was not enough to specify "infant death" as the outcome, since infant death is sometimes used to refer to stillbirths;[180 181]
- Stillbirth not mentioned (whether because they were excluded, or included but not found, or included and found but not reported);
- Stillbirth numbers or rates not reported separately from other outcomes;

- Stillbirth numbers or rates not stratified by race/ethnicity;
- Stillbirth only mentioned as a confounder/covariate (e.g., prior pregnancy loss);
- Only deaths included (only stillbirths, only stillbirths and newborn deaths), or case-control study with stillbirths as cases;
- Stillbirth included but none found;
- Grey literature (e.g., dissertations);
- Non-U.S.;
- Review (systematic, narrative, etc.).

Snowball review: A single reviewer (SHL) reviewed titles/abstracts of (1) reports mentioned in editorials and other non-studies that were excluded during phases 1-3 of title/abstract screening, (2) all relevant reports included in reviews that were excluded during phases 1-3 of title/abstract screening, and (3) reference lists of reports included via full text review.

Review of reviews: The following process was followed to review included papers of systematic and other literature reviews:

- Full text obtained
- For reviews which provided tables of included studies (such as systematic and scoping reviews), only those studies were reviewed.
    - If such a review stated that it had separated studies on stillbirth or fetal death from studies on other outcomes, or if "stillbirth" was listed anywhere in a table of included study outcomes, the review's criteria were followed
    - Meta-analyses were searched for stillbirth stratified by race/ethnicity
- For reviews with no identifying information on included papers, the following terms were

searched to identify any relevant studies referenced: stillb, still b, miscarriage, abortion, termination, fetal, perinatal, demise, death.

- For reviews that were specifically on stillbirth, the following terms were searched: race, racial, ethnic*, minorit*, disparit*, inequit*, equity.

Title/abstract review of snowball citations: Reference lists of reports included via full text review were reviewed for additional reports for possible inclusion via a two-step iteration: reference lists of reports that were included after full text review were checked; 30 reports were identified in this way for inclusion; their reference lists were also checked, yielding an additional four reports for full text review.

Data extraction: SHL drafted a data extraction tool and piloted it with EL on three studies, revised and then piloted on three more. It was then decided a third extractor was needed in the interest of time. SHL, EL and AC triple-extracted two studies.

For extraction of data for selected SDRs, in the case of multiple ratios being available, we used the following rubric to select a single one:

- Use estimate from the whole study sample, if available; otherwise, use estimate from the largest subgroup (for example, an estimate in full-term rather than preterm births was preferred);
- Where estimates from multiple years were available, we extracted from the most recent year or period;
- Where this rubric did not cover the specifics of the situation, we discussed and agreed on a case-by-case basis which data to extract.

For studies that reported stillbirth estimates from regression analysis, if race was the exposure, the SDR was considered to be equal to that estimate. If race was not the exposure, but

the report provided ratios of racial/ethnic minority stillbirth estimates to white stillbirth estimates, or if regression was not performed but stillbirth rate ratios comparing minority to white stillbirth rates were reported, then the SDRs was considered to be equal to these ratios. Otherwise, we calculated the SDRs ourselves from the available estimates and rates. (We reported not only the SDRs themselves, but also all data that we used to perform any required calculations.) We did not approximate data from figures (figures were only used if precise numbers were included).

We excluded 75 Black-white SDRs and three SDRs for other race group comparisons from SDR analyses, as the data were duplicated, but retained them for review of domains of analysis and explanation. These exclusions resulted in one of the 84 reports with Black-white SDRs being excluded from racial disparity analyses.[135] These SDRs were mainly for SBRs in single years, e.g., 2006 national stillbirth data presented in several U.S. government reports. For extraction of comments on racial disparity in stillbirths:

- only comments that related explicitly to racial disparity in stillbirths, or to racial disparity in composite outcomes that clearly included stillbirths, were included; e.g., possible explanations for the observed disparity, mechanisms, etc.
- no comments related to confounding, study limitations, reasons for possibly spurious findings, etc. (e.g., differential reporting of fetal deaths) were included.
- no comments related to explanations from other studies were included, e.g., in discussions of results in comparison with the literature, unless these explanations also appeared to represent the viewpoint of the study's authors.

Domains included:

- Genetic:
    - Including any references to genetic or other biological differences
- Fetal:
    - Including low birthweight, gestational age, birth year
- Maternal:
    - Including behaviors such as smoking
    - Innate characteristics such as age
    - Conditions such as pre-eclampsia
    - Prenatal care when it related to maternal decisions or preferences (e.g., “mother only attended two prenatal sessions”)
- Family:
    - Including paternal characteristics other than race (e.g., “father’s education”)
    - Any references to other family members
- Community:
    - Including comments on the neighborhood (e.g., “poor neighborhood”)
- Health system:
    - Prenatal care when it related to the system’s provision of care (e.g., “no clinics available near the residence” or “poor quality care provided”)
- Structural:
    - Including comments about policies, racism, multiple sectors other than the health system itself (e.g., “structural racism” or “segregation” or “multiple high-level factors interacting with each other”)

See Table A2 for further details.

Analytical approach: To summarize domains of analysis and explanation, categories were combined to ensure each had a count of at least 5 (see Table A13).

To calculate 95% CIs for SDRs for reports presenting stillbirth rates only (no regression estimates), we needed numbers of stillbirths and numbers of total births separately for Black and white births. In several cases, we had to calculate one of these quantities from published stillbirth rates. In a few cases, our estimates for stillbirth rates in Black and white births based on numbers of stillbirths and total births differed slightly from published estimates.

Additional details of methods for Chapter 3

Study population and data sources: New York City was selected as the location for this study because New York State has one of the highest stillbirth rates in the U.S. (8.3 per 1000 total births), and stillbirth rates in the counties of NYC are the highest in the state.[430] Further, NYC has high segregation as compared to other U.S. metropolitan areas. A U.S. Census Special Report on segregation found that NYC was the 8th most segregated overall of 43 metropolitan areas in 2000 for Black Americans, the most segregated using the Index of Isolation, and the 3rd most segregated using the Index of Dissimilarity. Ranking cities by the percent change in segregation indices between 1980 and 2000, NYC had the second-worst performance overall, and was the worst performer according to the Index of Dissimilarity and the 6th worst according to the Index of Isolation.[227]

The study population excluded multiples; however, four births with unknown multiple status were retained. A total of 334 stillbirths and livebirths were missing information on mother's residence, or mother's residence was within NYC but did not map to a PUMA (e.g., parks and airports).

The rationale for using ACS five-year rather than one-year datasets was that data at census tract level, which were required for the construction of the Indices of Dissimilarity and Isolation, are only provided for five-year estimates. Additionally, data reliability is greater in the five-year estimates.[431]

We received from DOHMH, and subsequently merged, 10 datasets for livebirths and 10 datasets for stillbirths, one per year.

Exposures: *Segregation measures – overview*: Segregation is the geographic separation of a population by group, e.g., by race or ethnicity, often into areas of low resource and

opportunity.[193] There are different types of segregation, including school segregation (when students are separated into different schools by race), workplace segregation (when workers are separated into different workplaces by race), and residential segregation (when individuals are separated into different residential areas by race). Segregation occurs in part by personal choice, for example when individuals make residence choices based on proximity to people of the same race. Segregation is also considered to be a proxy for, or manifestation of, structural racism (for instance see this systematic review of measures used to study structural racism,[206] which found that segregation indices were the most commonly-used measures of structural racism). Negative effects of segregation on health have been studied for over 70 years (for instance [152]). There is substantial epidemiological evidence for associations between segregation and adverse health outcomes (for instance [207]), and for different magnitudes and directions of associations according to race (for instance [199 208 209]). For these reasons, we selected segregation as one of the structural racism dimensions for the present study.

From the 1940s to the 1980s, segregation was commonly measured by the Dissimilarity Index. In 1988, Massey and Denton analyzed 20 existing measures of segregation (although they did not include an older formula for the Dissimilarity Index which they had published on in 1987).[212] They hypothesized that segregation can best be represented by five overlapping yet distinct domains (Table A41). Using data from the 60 largest metropolitan areas in the U.S., they carried out factor analysis on the 20 measures to assess (a) whether five domains in fact appeared and were distinct, and (b) which measures most strongly correlated with each domain. Finally, they selected one measure for each of the five domains, confirming their selections with principal components analysis (Table A42). (Of note, the measure they selected to represent the domain of evenness was a newer version of the Dissimilarity Index. Both older and newer

versions continue to be used, both are referred to as the Index of Dissimilarity, and both are occasionally cited as being from Massey and Denton 1988, though that paper does not mention the older version.)

In 1996, Massey and Denton repeated their factor analysis using a larger dataset including all 318 U.S. metropolitan areas, concluding that the data still supported the existence of five distinct domains of segregation and their choice of one 'best' index to measure each domain.[422] The influence of Massey and Denton's original model of segregation measures is strong; for instance, the U.S. Census 2000 Special Report "Racial and Ethnic Segregation in the United States 1980-2000" produced segregation estimates using indices in all 5 domains, including the indices recommended by Massey and Denton in 1988 (Table A42).[227] However, few studies have used all five indices, and some studies of segregation and health continue to use the traditional, single measure of segregation—the Index of Dissimilarity. This includes one of the two studies on segregation and stillbirth (Table A43).[81 214]

We found some differences between the results from the two Massey and Denton analyses, including increases and decreases in factor loading for measures of three of the five domains, evidence that three of the five factors mapped to more than one domain, and different factor mapping patterns for different racial/ethnic groups (Table A44).

Indices of Dissimilarity and Isolation: The present study included two measures of segregation, the Isolation Index (for the exposure domain) and the Dissimilarity Index (for the evenness domain). These domains and indices were selected for several reasons: they were found in the U.S. Census report to be strong indicators of segregation in NYC among Black Americans in 2000; a 2016 study of residential segregation and all-cause mortality in the U.S. found that these indices were more strongly associated with mortality than indices from other dimensions;

Kramer and Hogue found that under certain circumstances, all five segregation domains collapsed to these two;[214] and finally, these were the only segregation measures used in the two extant studies on segregation and stillbirth.[432]

The formula we selected for the **Index of Dissimilarity** for our main analysis was the version used by Williams et al. and others; the other version of this Index was used in a sensitivity analysis, with the expectation that results would not differ depending on the formula.[64 221 419-421] Population data for race/ethnicity were aggregated from the census tract level to the level of the PUMA using the mapping provided at www1.nyc.gov, the official website of the government of New York City, which maps census tracts to PUMAs using 2010 geographical borders. The minority population was defined as all individuals identified by the ACS as non-Hispanic Black/African-American, the white population as all non-Hispanic white individuals, and the total population as all individuals regardless of race/ethnicity.[64 227]

For construction of the **Index of Isolation**, although the original conception required that "total" be defined to include all individuals regardless of race/ethnicity,[212] and this has been followed by some (e.g., the Brookings Institution), researcher practice has been to include just totals of Black and white individuals (including in the U.S. Census study on segregation);[199 209 227 237] this definition was therefore used for the main analysis in the present study, and in a sensitivity analysis, "total" was defined as all individuals regardless of race/ethnicity.

Index of Concentration at the Extremes (ICE)*:* A critique of the segregation indices reviewed and proposed by Massey and Denton was their "aspatial" nature. Reardon et al. argued that segregation measures must both define an individual's social environment and quantify how individuals' experiences differ across those environments, and that since most extant segregation measures use pre-defined geographical areas such as census tracts to define the social

environment, they do not sufficiently account for the spatial nature of segregation.[215] They proposed a new set of 'spatial' indices of segregation, which were intended to address specific issues they identified as being associated with aspatial measures, such as the 'checkerboard problem' and the modifiable areal unit problem (MAUP).

The 'checkerboard problem' is that most segregation indices are only focused on distributions of individuals within neighborhoods, yet segregation can also manifest as uneven distribution of the neighborhoods themselves. However, it is precisely this issue that is addressed by indices for the clustering domain, such as the spatial proximity index (Table A42).

Meanwhile, the MAUP is not an issue unique to segregation studies. It is relevant for any research that involves the study of individuals within groups (e.g., whenever a group-level exposure is chosen). The issue is that results depend on how the groups are defined. It could be argued that this issue applies to all studies, since all studies are of a group (the study population), and results necessarily depend on how that group was defined. Reardon et al. make the point that using, for example, census tracts as the unit of measurement for a segregation index implies that the experiences of individuals within one census tract yet at opposite ends of it will be more similar than the experiences of individuals in two census tracts who live on opposite sides of their shared border. However, this is true any time data are allocated into groups—including when variables are categorized in any way.

Reardon et al. state that "[i]n principle, a segregation measure that used information on the exact locations of individuals and their proximities to one another in residential space could eliminate the checkerboard problem and MAUP issues entirely."[215] However, they acknowledge that in practice, spatial segregation measures may still require researchers to choose arbitrarily bounded areas, such as census tracts, since "tract boundaries and contiguities are generally used

to approximate spatial distance." Indeed, they point out that some "aspatial" measures of segregation are just special cases of "spatial" measures when the underlying, often unstated assumption of "aspatial" measures is articulated: that "the local environment of each individual [is] … equivalent to the organizational unit (e.g., census tract, school) containing the individual."[215]

We were not able to identify any studies of adverse birth outcomes which used Reardon et al.'s spatial segregation measures,[214] though other measures of spatial segregation have been used (for instance [433] used in [434-436]). The majority of studies of adverse birth outcomes continue to use the measures recommended by Massey and Denton in 1988. However, in 2001 a new measure was introduced by Massey, the Index of Concentration at the Extremes (ICE). The index was intended to address persistent limitations in sociology, including its focus on poverty rather than the interplay between poverty and wealth, and its focus on individual neighborhoods rather than interactions between neighborhoods.[216] Hence, ICE addresses some of the limitations of more established indices which had driven the earlier push to create spatial segregation measures—and it does so using a formula that is easy to calculate and intuitive to interpret. It has been described as a measure of spatial social polarization.[217]

ICE allows the user to define "most privileged" and "least privileged" (also referred to as "privilege" and "disadvantage") using multiple characteristics, for instance race and income, thereby modelling not only residential segregation, but what has been termed racialized economic segregation,[218] and incorporating what Massey termed the "interactive" effects of individual and neighborhood disadvantage.[216] Because any quantifiable characteristics of a population can be incorporated into the measure, ICE can represent multiple domains (thus also addressing potential problems related to collinearity of separate measures).

The use of ICE has been gradually increasing in research on segregation and public health, for instance in studies of all-cause mortality[219], cancer[220] and assault[221]. ICE has been recognized as a measure of structural racism (e.g., in this study of infant mortality[218]) and has been used in studies of adverse health outcomes by the NYC DOHMH (e.g., on infant mortality and preterm birth[222] and neonatal morbidity and mortality[223]), who provided the data for our study.

For our study, ICE was constructed defining 'most privileged' as both white non-Hispanic and high-income, and 'least privileged' as both Black and low-income. Household race/ethnicity is assigned by the ACS based on the race/ethnicity of the householder, with just one householder per household. The ACS does not disaggregate household income data or educational attainment data by ethnicity for Black individuals, hence Black rather than non-Hispanic Black was used in construction of ICE (and the Educational Inequity Ratio).

Following recent use of ICE in Massachusetts[221], Chicago[218], and NYC[223], we defined high- and low-earning households as those earning ≥$100,000 and <$25,000 per year, respectively. In a sensitivity analysis, high- and low-earning were defined as ≥$200,000 and <$35,000. There has been variation in approaches to whether the ICE denominator includes all individuals[221] or just the sum of most and least privileged individuals[222 223] in a given neighborhood. For this study, the original definition, which includes all individuals in the denominator, was used.

Choice of group level at which to measure segregation: The main consideration for choosing the group level at which to estimate the association between structural racism and stillbirth was availability of birth location data to allow mapping of births to group-level exposures. Since stillbirth is a rare outcome, there are small numbers of stillbirths in each census

tract. Hence, for confidentiality purposes, census tracts were not provided for the births used in this study. Instead, each birth was identified by PUMA of mother's residence (or in some cases by community district, which maps to PUMA). Therefore, exposures also had to be measured at the PUMA level.

There have been critiques of measuring segregation at this level. Gee et al. questioned whether segregation is usefully measured at any lower level than the city, given that reducing structural racism requires structural interventions,[193] while Krieger et al., who saw the dearth of studies on segregation and health at within-city levels as an important research gap, stated that the Index of Dissimilarity and other similar indices "cannot be meaningfully used at lower levels of geography on account of spatial social segregation," arguing instead for the use of ICE to overcome this problem.[217] However, Massey and Denton argued that "[census] tracts represent the best and closest practical approximation to the concept of 'neighborhood'" and also are the most common basic areal unit used in constructing segregation indices, so choosing census tracts also helps to increase comparability of data across studies.[422] Moreover, they argued that associations will be stronger at the local level since populations tend to be more homogenous the more locally they are defined,[215] so analysis at higher levels risks "underestimating the adverse impact of segregation on health."[221] The U.S. Census report assessed segregation at the metropolitan area level. Metropolitan areas have a population of at least 50,000 and so are comparable in size to PUMAs which have at least 100,000 people each. Finally, measuring the exposures at the PUMA level could also possibly help address any bias associated with mothers shifting residence between year of exposure measurement and year of delivery, since the larger the geographic unit, the smaller the number of mothers moving out of it, all else equal.

Another potential issue with the choice of level for this study, which included 10 years of

data but measured exposures as averages over two five-year periods, is changes over time in the boundaries of the geographical areas used to construct the exposures. For instance, "[census t]racts are sometimes added, split, or combined between censuses", and this is sometimes differential across race, with a tendency for newer tracts to be more racially homogenous.[227] However, this was unlikely to be a concern, as the boundaries of ACS geographic areas for the two five-year vintages are defined as those reported by the U.S. Census as of January 1 of 2013 and 2018, respectively, and for both of these vintages, the Census in question was the 2010 Census, hence the geographic boundaries used in both vintages were identical.

Operationalizing the exposures: Following the literature, ICE was split into quintiles and the other exposures into tertiles. Two values of each exposure were calculated for each of the 55 PUMAs, one for each vintage. Structural racism exposures (as well as PUMA-level covariates) were mapped to individual births using PUMA of maternal residence and year of birth ("2013" data were mapped to births in 2009-2013 and "2018" data were mapped to births in 2014-2018; see Table A15).

Covariates: *Birth characteristics*: **Sex** was coded as male, female, or missing (all unknown and undetermined sex were conservatively recoded as missing). **Gestational age** was recorded as the clinical estimate of gestational age in completed weeks. **Birthweight** was recorded in 100 gram increments, except for the lowest category which was 0-50 grams, and which was set to missing for our study. The next lowest category of 50-150 grams (coded as "100 grams") was plausible for 20 week stillbirths, but the six livebirths with this birthweight were recoded to missing birthweight as well.

Maternal characteristics: **Maternal race/ethnicity** was coded as non-Hispanic Black, non-Hispanic white, non-Hispanic Asian (including Native Hawaiians and Pacific Islanders),

non-Hispanic Native American (including Alaskan Natives), Hispanic, other (including those with other single race and with two or more races), and missing. Non-Hispanic racial/ethnic groups included those with missing data on Hispanic ethnicity. **Maternal education** was only available as a categorical variable, coded as high school graduate or less, any college, and higher than BA. **Maternal age** was recorded both continuously and as a categorical covariate: <20, 20-34, and 35+. **PNC visits** were recorded as a continuous covariate.

Eight **maternal conditions** (chronic hypertension, gestational hypertension, chronic diabetes, gestational diabetes, sexually transmitted diseases (STDs), hepatitis, cardiac disease, and other risk factors) were coded according to the algorithm in Table A45 which shows how we combined covariates from three different sets of data recording instruments (for livebirths 2009-2018, for stillbirths 2009-2010, and for stillbirths 2011-2018). There were separate binary covariates for each of these eight conditions for all livebirths 2009-2018 as well as stillbirths in 2011-2018, but for stillbirths in 2009-2011, maternal conditions were recorded in a set of six covariates, each of which had the same list of 23 risk factor options (first column in Table A45). Hence, stillbirths in 2009-2010 could be reported as having a maximum of six of these 23 risk factors. Further, many maternal conditions were not reported in the same way in the three data recording instruments, or were present in one or two but not all three data recording instruments. Maternal conditions in the final merged dataset for our study were recorded as No if (a) No for the individual condition for livebirths 2009-2018 and stillbirths 2011-2018 or (b) No for all 6 summary covariates (meaning no maternal condition of any kind, rather than no to the specific maternal condition in question) for stillbirths 2009-2010. The “other risk factor” covariate was Yes if any of the conditions mentioned was present, and missing otherwise (as none of the components of this covariate was available in all three data recording instruments). Finally, the

eight maternal conditions were merged into a single composite covariate representing the presence or absence of any of the eight separate conditions.

All unknown values for all birth and maternal characteristics were recoded to missing, except for maternal age which was missing for only five births.

Group-level characteristics: The NYC Center for Economic Opportunity (CEO) poverty thresholds were used, as they are specific to the city. For 2013, the threshold was $31,156 and for 2018 it was $35,044, both higher than the poverty thresholds used by the U.S. Census.[437 438] (Because the CEO also uses a different definition of income from the U.S. Census, CEO poverty thresholds were not used for construction of the ICE structural racism measure.) **Poverty** data were mapped from community district to PUMA. For the group-level measure of **educational attainment**, we used ACS table B15003 for vintages 2013 and 2018. This table reports the proportion of PUMA residents 25 years or older with at least a GED or high school diploma (following Brown et al.[81]). The **minority proportion** of the PUMA population was calculated as the number of non-Hispanic Black residents divided by total number of residents in the PUMA, also using ACS data.[230 232 213]

Analytical approach: Following Ward et al. and Williams et al., we established that the prevalence of both stillbirth and structural racism differs across race, and then explored whether associations between structural racism and stillbirth differ across race.[64 439]

Model specifications: All regression models used the following specifications to reduce processing time and assist with model convergence: nAGQ = 0 and control = glmerControl (optimizer = "bobyqa") (see https://rdrr.io/cran/lme4/man/glmer.html for more details). Z-scores for all continuous covariates and exposures were based on population and PUMA means for

individual-level and PUMA-level covariates, respectively. Age-squared terms were calculated by squaring the age Z-score.

Sensitivity analyses: Alternative versions of three of the exposures were used to assess sensitivity of the results to the way each exposure was constructed (see Table A14 for formulas):

- **Index of Dissimilarity alternative version**: The second of the two extant formulas was used; both formulas have been used in the literature and there is no consensus on the preferred version;
- **Index of Isolation alternative version**: Total population was defined as total in the census tract (regardless of race/ethnicity) rather than Black + white; typically Black + white has been used in similar studies, but the original definition of this Index suggests total population was intended to be used;
- **ICE alternative version**: Privilege was defined as non-Hispanic white households earning $200,000+ and disadvantage as Black households earning <$35,000; all relevant studies that we know of use the <$25,000/$100,000+ distinction instead, including all the studies using ICE in NYC and NY State; nonetheless, the <$35,000/$200,000+ distinction more closely reflects NYC poverty and wealth levels.

Additional details of methods for Chapter 4

Data source and study sample: SCRN aimed to enroll a racially and ethnically diverse group of mothers from both urban and rural areas of the U.S. that would be large enough to ensure a sufficient sample size for race- and gestational age-specific analyses. SCRN staff constructed analytical weights to account for differential sampling and participation using a generalized exponential model which estimated the propensity to participate; the weighted cohort included 663 stillbirths and 1,439 livebirths.[270] Placentas were collected and stored at birth by labor and delivery staff in accord with SCRN's standardized examination protocols. SCRN pathologists conducted exams, aiming to complete macroscopic examinations within three working days. Four samples of approximately 2 grams each were collected for freezing from the maternal side of the placental parenchyma using a random sampling method under the direction of SCRN anatomic pathologists; one of these samples was frozen at -80° Celsius for later studies requiring DNA extraction.[440] Alternate procedures were followed for multiples and fragmented placentas.

While none of the 63 stillbirths included in the study had an anomaly as reported within the original SCRN dataset, a subsequent study of causes of death for 512 stillbirths in SCRN did identify one of the stillbirths as having a 'probable' genetic cause of death (confined placental mosiacism and small for gestational age).[57] This was also one of the two samples that were flagged as outliers; we excluded it in a sensitivity analysis.

Outcome and exposures: *Outcome*: Stillbirth was defined by SCRN as birth at 20 or more gestational weeks with an Apgar score of 0 at both 1 and 5 minutes with "no other signs of life by direct observation", or if born at 18 or 19 gestational weeks "if not well dated" and met all other criteria (Supplementary Materials, Tables, p.5[270]).

Index of Significant Life Events: The significant life events originate from the CDC's Pregnancy Risk Assessment Monitoring System (PRAMS).[271] A description of PRAMS from the CDC's website follows:

> "*The Pregnancy Risk Assessment Monitoring System (PRAMS) was developed in 1987 to reduce infant morbidity and mortality by influencing maternal behaviors before, during, and immediately after pregnancy. It is the only surveillance system that provides data about pregnancy and the first few months after birth. PRAMS is an ongoing, site-specific, population-based surveillance system designed to identify groups of women and infants at high risk for health problems, to monitor changes in health status, and to measure progress towards goals in improving the health of mothers and infants*." (accessed 4 Feb 2022)

PRAMS participating sites represent over 80% of U.S. livebirths (stillbirths are not included). The 13 significant life event questions have formed part of PRAMS questionnaires for over 20 years (included in Phase 4, 2000-2004, Phase 5, 2004-2008, Phase 6, 2009-2011, and with slight modification in Phase 7, 2012-2015, and Phase 8, 2016-2019). Numerous studies have used these to measure maternal stress and pregnancy outcomes, often grouping them into factors or constructs. While there are a variety of approaches to grouping, e.g., [441] [442], the most common approach has been to model them as four factors, termed emotional, financial, partner-related, and traumatic, after Ahluwalia et al. who named them after identifying them through principal components analysis in a study of stress and small for gestational age pregnancies.[272] Others have also used this approach.[273-277]

For the categorical version of SLE, we deviated slightly from Hogue et al. who broke SLE into 0, 1, 2, 3, 4, and 5+ events, instead breaking at the first, second and third quartiles

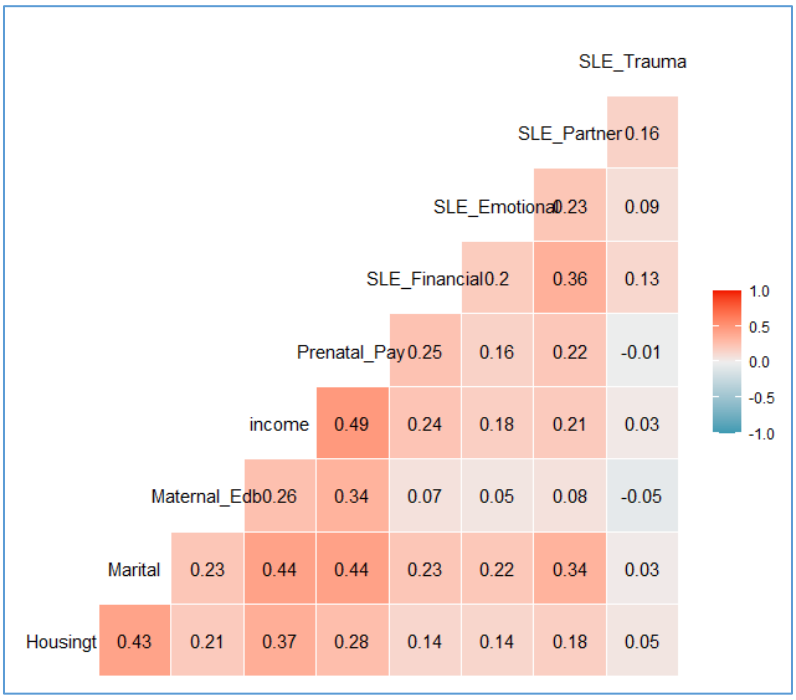
based on the distribution in SCRN (n=2703, see Table inset), resulting in the following categories: 0, 1, 2, 3, or 4+ events. The distribution of SLE in our study sample (n=189) was 0 items, n=47 (25%); 1 item, n=46 (24%), 2 items, n=32 (17%); 3 items, n=19 (10%); 4 or more items, n=35 (19%). Ten individuals in the study sample (n=5%) had no data for SLE (for any item).

Min	Q1	Median	Mean	Q3	Max	NA
0	1	2	2.2	3	12	158

We compared our covariates for total number of SLEs and presence/absence of each factor to the SCRN-created covariates. Due to apparent errors in the SCRN summary covariates (coding that did not align with SCRN explanations of coding decisions as stated in [443]), we used our versions of these covariates. Specifically, SCRN rules mandated that the "variable for the number of SLE factors, SLEfsum, [be] set to missing if there was a missing response for one or more of the 4 factors included in the sum", yet this rule was not followed for 25 records for the financial factor, two records for the emotional factor, and three records for the traumatic factor. Moreover, the literature does not provide any justification for this approach to counting factors (excluding records with missingness). There was also no justification in the literature for the approach to the SCRN total SLE item count, which "was set to missing if there was a missing response for one or more of the 13 items included in the sum", and in any case there were only very slight differences between it and our SLE crude item count, though there was a possible attenuation of estimates of association.

Index of Disadvantage: The range for the Index in the study sample (n=189) was 0-4, with only three individuals scoring 3, and two individuals scoring 4. Following Miller et al., we therefore collapsed Disadvantage to three categories: 0 items (n=117 individuals, 62%), 1 item (n=50 individuals, 26%), and 2 or more items (n=22 individuals, 12%).[278]

Maternal education was measured in years.[444 445] **Housing status** was recorded by SCRN as rent; own; live with family, friends, or in-laws; shelter; or homeless. A related covariate captured, for individuals who rent or live with others, whether this was in public housing. We combined these into a three-level covariate: any public housing (including shelters) or homeless; living with family, friends, or in-laws other than in public housing; and rent (other than in public housing) or own.[446-448] **Family income source** over the last 12 months was coded by SCRN as only public/private assistance; both assistance and personal income; and only personal income. Other federal, state and local government assistance programs were considered to be public assistance; private charities (e.g., hospital/faith-based charities) and help from friends/family were considered to be private assistance; and additional income from the father, disability for maternity leave, and financial aid/scholarships were considered to be personal income. **Prenatal pay** source was coded by SCRN as no insurance; any public/private assistance; and Veterans Affairs/commercial health insurance/health maintenance organization. SCRN collected two relevant variables for **partnership** status: whether married or not, and whether living with a partner or not. We created a single covariate to indicate whether not cohabiting (including those who are married but not cohabiting); cohabiting and not married; or cohabiting and married.[449-



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See Figure inset for Pearson correlation coefficients between components of the two indices. Relatively low correlation suggests these are distinct constructs, supporting our additive approach for building the indices.

Covariates: *Livebirth/stillbirth characteristics*: **Sex** was male, female, or undetermined. We used the SCRN best estimates for **birthweight** ("from chart abstraction, unless for a stillbirth, the weight reported by the pathology lab was greater. In this case, the weight reported by the pathologist was used"[443]) and **gestational age** (weeks from conception to livebirth delivery or stillbirth death, with portion of weeks expressed as a decimal[443 452]). **Prenatal care timing** was recorded as starting in trimester 1 (if first prenatal visit was in months 1-3 or weeks 1-13), starting in trimester 2-3 (trimester 2 was months 4-6 or weeks 14-27, trimester 3 was months >6 or weeks >27) or no prenatal care, or missing data.

Maternal characteristics: Ever smoking was yes if mothers reported any smoking or tobacco use up to two years prior to maternal interview (smoking status prior to this period was not available). Passive smoking was yes if cotinine concentration in maternal blood samples taken at delivery exceeded the SCRN-designated threshold for passive or second-hand smoke exposure (0.25 ng/mL or more). We combined these two covariates into one capturing **smoke exposure** that was yes if either ever smoker or passive smoking was yes, no if both were no, and missing otherwise. **Prior stillbirth** was yes if there had been any prior pregnancy loss of 20 or more gestational weeks or any prior pregnancy loss with unknown gestational age. **Pregnancy complications** was yes if any of 12 conditions had been noted in maternal charts as occurring during the delivery hospital visit itself (premature rupture of membranes, preterm labor, cervical incompetence, chorioamnionitis, preeclampsia/gestational hypertension, placenta previa,

placental abruption, non-reassuring fetal heart rate tracing, endometritis, other systemic infection, cord prolapse, or other unspecified condition), no if all of these were recorded as not occurring, or if the "none of these" box was checked, and missing otherwise. Of note, the "other" category included 1,111 free text responses with a wide range of conditions. **Pre-existing maternal conditions** was coded as yes if medical records recorded "Entered pregnancy with diagnosis of diabetes (not gestational)" or maternal interviews recorded the pre-pregnancy presence of any of 23 conditions (high blood pressure; asthma; seizure; diabetes; hyperthyroidism; hypothyroidism; valvular heart disease; other heart disease; coronary artery disease/congestive heart failure; kidney disease; sickle cell anemia; thrombocytopenia; lupus; antiphospholipid antibody syndrome; rheumatoid arthritis; colitis/Crohn's; cholestasis; cancer; sexually transmitted diseases: gonorrhea, chlamydia, herpes, syphilis, HIV/AIDS, hepatitis B, hepatitis C, other; mental health condition; urinary tract infection[95]; blood clots/stroke; or "other" (up to 2 conditions)). (There were no data on medication use for these conditions.)

Maternal gestational conditions was yes if any of eight conditions had been recorded as present in maternal charts (we chose these as they are well-known risk factors for stillbirth[44 95]), or if any had been reported during maternal interview as

Box: Maternal gestational conditions

Yes if any of the following (whether or not medicated for the condition):

1. diabetes
2. hypertension/high blood pressure
3. hypothyroidism or hyperthyroidism
4. sickle cell anemia
5. any STD (e.g., HIV/AIDS, syphilis, hepatitis B/C)
6. psychiatric disorder
7. cholestasis
8. urinary tract infection

Yes if medicated for any of the following:

1. antiphospholipid antibody syndrome
2. asthma
3. blood clots/stroke
4. blood disease
5. coronary artery disease / congestive heart failure
6. cancer
7. cardiovascular conditions
8. colitis/Crohn's disease
9. connective tissue disorder
10. GI / liver disease
11. kidney disease
12. lupus
13. nephropathy
14. other heart disease
15. renal failure
16. rheumatoid arthritis
17. seizure
18. thrombocytopenia
19. ulcerative colitis
20. valvular heart disease
21. other condition

present during pregnancy, regardless of whether the mother had been medicated for the condition, or if any of 21 additional conditions were reported in charts or maternal interview as present during pregnancy and mother had been medicated for the condition(s) (see Box inset). If all these conditions were reported as absent, or present but (in the case of the 21 additional conditions) not medicated, this covariate was coded as No; otherwise as missing. We cross-checked both maternal gestational conditions and pre-existing conditions against SCRN constructed variables for specific conditions and found some errors which required recoding.

Production of methylation data: ***Overview of the process of obtaining methylation data*****: First**, DNA is extracted from biological samples. Since each cell has two copies of each autosomal (non-sex) chromosome, each cell also has two copies of a given gene, and hence two copies of every CpG. A single sample from the placenta, with ~500 ng of genetic material, will have tens of thousands of cells of different types. (For context, there is about 1 ng of DNA in 200 human cells.) Therefore, the sample will also have tens of thousands of copies of each CpG. The extracted DNA is tested for quantity and quality, and samples are normalized, so that concentrations of DNA are the same.

Second, bisulfite conversion is performed. DNA methylation occurs when a methyl molecule binds to the cytosine base of a cytosine-guanine base pair (CpG). Bisulfite conversion is a process whereby unmethylated cytosine bases are converted to uracil, which after PCR amplification get converted to thymine bases. Meanwhile, methylated cytosine bases remain unchanged. The DNA is then denatured, meaning that it is converted to single strands, and transferred onto chips (microarrays). Each chip is covered with many probes, which are also single-stranded fragments of DNA about 25 nucleotides long, each complementary to a specific CpG. Illumina's MethylationEPIC microarray that was used for this study has probes that are

complementary to about 850,000 CpGs, comprising just 3% of the 28 million CpGs in the human genome, but covering many key regions including >95% of CpG islands, as well as CpGs on gene bodies and in enhancers and promoters.

Third, the chips are loaded into a hybridization chamber. Overnight, the single-strand sample DNA fragments bind to the single-strand probes. The chips are then washed to remove unbound DNA, stained with fluorescent red or green dye in a flow cell chamber, and dried for 24 hours.

Fourth, dye color and intensity are analyzed by a scanner and translated into beta values. A DNA sample from one individual has tens of thousands of cells, each with two copies of every CpG. Hence, while the methylation status of a single CpG on a single chromosome is binary, an individual's methylation status for that CpG is represented as the percent of all probes for that CpG that record methylated copies of that CpG. Beta values approximately equal the percent of all copies of a CpG that are interpreted as being methylated; therefore beta values range from 0 to 1. Hence, ultimately, methylation assays identify, for the subset of CpGs for which the microarray has complementary probes, what proportion of all the copies of a given CpG in a single sample are methylated.

DNA extraction, bisulfite conversion and microarray processing: According to SCRN's standardized examination protocols, placentas were collected and stored at birth by labor and delivery staff from all stillbirths and livebirths for whom consent had been obtained; SCRN pathologists conducted exams, noting whether placentas were fresh or fixed, and aiming to complete macroscopic examinations within three working days. Four samples of approximately 2 grams each were collected for freezing from the maternal side of the placental parenchyma using a random sampling method, under the direction of SCRN anatomic pathologists according to

standardized placental examination protocols; one of the four samples was frozen at -80° Celsius for later studies requiring DNA extraction.[440] Alternate procedures were followed for multiples and fragmented placentas. For this study, the DNA Extraction Facility at the Clinical and Translational Science Institute, University of Utah, isolated DNA from frozen placental samples according to their lab protocols. Bisulfite conversion was performed using the Zymo EZ DNA Methylation Kit (Zymo Research Corp., Irvine, CA) according to the manufacturer's protocol for array platforms.[453] The recommended modification to the protocol was performed. The final DNA elution was transferred to the Illumina EPIC microarray platform.

We specified the order of the samples across the plates in order to reduce the chance of batch effects. We randomly allocated half the stillbirth samples (cases) and half the livebirth samples (controls) from each of the five sites to either Plate 1 or 2. Each plate has 96 wells divided into 12 columns and eight rows; each column is loaded onto a separate array (or "chip"). Hence, each chip has eight wells. Plate 1 was filled and Plate 2 had three empty wells. For Plate 1, we randomly selected 32 cases and 64 controls; we randomly allocated 24 of these cases and 60 of these controls to chips in groups of two cases and five controls respectively; then the remaining four controls were allocated randomly to one of the 12 chips and the remaining 8 cases were allocated randomly to one of the eight chips that still had an empty well. For Plate 2, we performed the same process, except that there were only two remaining controls which were allocated randomly to one of the 12 chips, and the remaining seven cases were then allocated randomly to one of the 10 chips that still had an empty well.

We then randomly allocated the cases or controls to a specific well on the assigned chip. Finally, we reran the entire allocation with a different seed to obtain a more balanced sex distribution. Positions were labelled by Plate (2 plates, 1 or 2), Row (8 rows, A-H), and Column

(12 columns).

The Genomics Core Facility, University of Utah Health Sciences Center, processed samples with Illumina's Infinium HD Methylation assay protocol – manual method using Illumina MethylationEPIC v1.0 arrays. A test run of 16 samples (columns 11 and 12 of Plate 1) showed good signal intensity and no quality control flags. Processing and scanning occurred between May 6 and 21, 2021. The raw .idat files were then made available to us via the University of Utah's UBox dropbox.

Methylation data preprocessing and quality control: Pre-processing and quality control of methylation data includes numerous steps which are focused on (a) identification and flagging or removal of failed probes (probe filtering), and (b) adjustment of beta values for several sources of bias. Unless otherwise noted, the R package ewastools was used for these steps. Details follow:

- **Assessed sample quality**: The Illumina microarray comes with 17 quality control summary metrics which are used to identify any samples for which microarray processing failed; these samples would then be excluded. We verified that none of the 189 samples failed.
- **Checked sample identity**: We checked sample identity by generating predicted sex based on sample genotype and comparing it to recorded sex. Stillbirths/livebirths with X chromosome intensities close to 1 and low Y chromosome intensities were predicted to be female, while those with lower levels of X and high Y chromosome intensities were predicted to be male. We found 6 sex mismatches: one recorded as male was predicted to be female; the others were the reverse. One possible explanation for the identified sex mismatches is that predicted sex was wrong, e.g., if something happened during sample

processing (other than contamination), however, each of these six samples was on a different chip, so this was unlikely. Another possible explanation is that recorded sex was wrong; however, University of Utah staff doublechecked these samples and verified that they did not appear to be mislabelled; we also checked with two researchers at the University of Utah who have worked with some of the SCRN biospecimens to see whether there were any overlaps on our sex mismatches that could shed light on the issue, but there were not. We excluded the sex mismatches from all regression analyses.

- **Identified and removed failed probes**: There were 205,833 probes whose probability of being detected was no different from background noise using the default *p*-value cut-off of 0.01 (probes for which both methylated and unmethylated intensity levels were recorded as 0).[454] These were set to missing for the affected samples, representing about 0.13% of all probes across all samples. This compares favorably with typical performance, with failed probes commonly comprising up to 10%.
- **Adjusted for dye and probe type bias**: Methylation of each CpG is determined by one of two different types of probes: "Type I" and "Type II". CpGs interrogated by Type II probes have methylated and unmethylated levels determined by green and red dyes using a single probe, while CpGs interrogated by Type I probes have two probes that determine methylated intensity and unmethylated intensity separately. The dyes and probe types both have known differences that were normalized per standard protocol.[455]
- **Identified and flagged outliers**: We flagged two samples with average log odds of belonging to the outlier component across all SNP probes that exceeded -4. This could indicate degraded or contaminated samples. These were subsequently excluded in a sensitivity analysis.

- **Assessed batch effects**: To check for batch effects, we removed XY chromosomes and SNPs, and then performed principal components analysis on the remaining beta values and assessed associations between the first two principal components and (a) plate and (b) row using linear regression. There was modest evidence of an association with plate so we adjusted for plate in all regression analyses involving methylation.
- **Identified and removed probes for CpGs with known SNPs and cross-hybridizing probes**: Using the R packages DMRcate and MethylToSNP, we identified and removed probes for CpGs known or suspected to be influenced by single nucleotide polymorphisms (SNPs), including 16,241 SNP-related CpGs and 309 probes with SNP-like patterns. We also removed 44,514 known cross-hybridizing probes (those which bind to more than one CpG), as they cannot reliably reflect methylation at a unique CpG.
- **Obtained predicted cell type proportions**: Given that the placental samples contain a mixture of cell types, each with a different methylation profile, it was necessary to enable adjustment for cell type composition. Using a prediction model for full-term placentas that includes six cell types (trophoblast, stromal, Hofbauer, endothelial, nRBC, and syncytiotrophoblast), the predicted cell composition of each of the 189 samples was recorded.[262 423 456]

Selection of candidate genes and CpGs: Following a non-systematic literature review in PubMed through which we identified 45 potential candidate genes, we carried out a backward search of these genes to identify a subset for which:

- There was evidence of association with relevant exposures and/or outcomes in more than one study (we excluded post-traumatic stress disorder, major depressive disorder, and outcomes after the neonatal period);

- At least one of the relevant studies used placental tissue; and
- The gene is known to be expressed in the placenta.[457]

We excluded 40 genes for the following reasons:

- Two genes excluded (*H19* and *MEST*)[269 285 293]: placental results borderline;
- 10 genes excluded (*AVP, CCL1, CD1D, F8, KLRG1, NLRP12, OXTR, SLC6A4, SNRPN, TLR3*)[293 294 303-305 346 449 458-460]: relevant exposures/outcomes, >1 study, but none found in placental tissue;
- 11 genes excluded (*ANKFY1, CRH, CRHBP, EEF1B2, EPB41L4B, HSD11B1, IGF1, INPP5E, KCNQ1, SMAP1, TM6SF1*)[264 269 287 289 343]: relevant exposures/outcomes, in placental tissue, but just one study found;
- 17 genes excluded (*CRF, CYFIP1, DNMT1, DNMT3A, GABBR1, GNASXL, GRIN2B, IL6, LIT1, MBD2, MEG3, MTHFR, PEG3, PYDC1, SLAMF7, TET3, TLR1*)[288 293 294 304 305 345 348 461-465]: relevant exposures/outcomes, but just one study found, placental tissue not used.

We included all CpGs that were either on the body of one of the five candidate genes (between the genomic start and end points using build 38) or on promoters and enhancers for these five genes as identified by GeneCards (selecting regions that had been mined from both ENCODE[466] and Ensembl,[467] two prominent genomic libraries).[468] Promoters may lie on the gene body or upstream (toward the 5' end of the chromosome from the gene body), and enhancers may lie upstream or downstream (toward the 3' end of the chromosome from the gene body).

Analytical approach: *Associations between maternal stressors and stillbirth*: In this case-control study design, the exposure odds ratio that is estimated is mathematically equivalent

to the disease odds ratio; hence for convenience we refer throughout to the odds of the outcome, stillbirth, with a change in the exposure, stressors.[315] Prentice and Pyke provide a proof of equivalence of the prospective logistic model, specifying Pr(D=i|z), and the retrospective logistic model, specifying Pr(z|D=i), where in our case i=(stillbirth, livebirth), and z is the regressor vector including the exposure and other covariates. For our purposes, the relevant portion of the proof is its extension (in section 6, equations 13 and 14) to the situation in which cases and controls are sampled from strata s=s(x), where auxiliary variable x defines the strata, in our case just site. The prospective and induced retrospective logistic models are specified as Pr(D=i|z,s) and Pr(z|D=i,s), respectively, and again, the estimated regression coefficients are shown to be equivalent, proving that the prospective logistic regression model we specified estimates the odds of stillbirth with a change in stressor.

Race was measured in the SCRN dataset by maternal self-report (or chart abstraction or screening data if the interview was missing this information) which we collapsed into four categories: non-Hispanic Black, non-Hispanic white, Hispanic, and other.

***Screening of 1,191 CpGs*:** DMRcate requires selection of values for λ, which places a bound on the genomic length of possible DMRs, and c, a scaling factor that helps to determine whether and how CpGs are incorporated into DMRs.[469] We followed Mallik et al. who identified 500 and 5, respectively, as the best-performance settings.[470] Note that negative M-values indicate that <50% of CpG copies are methylated and positive M-values indicate that >50% of CpG copies are methylated.

We screened out CpGs and DMRs for which directions of effect in associations between stress and methylation, and methylation and stillbirth, were opposing. If *increased* stress were associated with *increased* methylation, and *increased* methylation were in turn associated with

increased risk of stillbirth, then increased methylation would be a plausible mechanism by which increased stress may raise the risk of stillbirth (with the reverse also true; i.e. reduced stress associated with reduced methylation, in turn associated with reduced risk of stillbirth). However, if *increased* stress were associated with *increased* methylation, but *increased* methylation were associated with *reduced* risk of stillbirth (negative association), then increased stress could not increase the risk of stillbirth through a methylation pathway (though it could do so through other pathways).

***Mediation analyses*:** The R Mediation package uses bootstrapping to estimate confidence intervals; we set 3000 simulations and used a seed for reproducibility.

In causal mediation analysis, the effect of the exposure on the outcome is broken down into its natural direct effect on the outcome via a pathway excluding the mediator (path c' in the Figure inset), and its natural indirect effect on the outcome via a pathway including the mediator (paths a and b in the Figure).