Birth weight, infant mortality, and race: Twin comparisons and genetic/environmental inputs

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Genetic and environmental inputs may shape population health disparities in varying ways. In this article, we use unique variation involved in twin births to attempt to untangle how genetic and prenatal environmental variation may make different contributions to infant health among white and black populations in the United States. Using twin fixed effects models and data from the 1995—1997 Matched Multiple Birth Dataset we compare birth weight—mortality associations across twin sex composition, zygosity, and race. Findings reveal suggestive differences between fraternal and imputed identical twin estimates for white and black twin pairs.

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Introduction

Gene—environment interactions present health researchers with complex empirical identification problems at the crux of the nature—nurture puzzle. When considering health disparities across social groups, researchers face the additional complexity of social structural variables and inequalities. An ongoing puzzle for social epidemiology is how unequal social conditions across categories of stratification (e.g., race—ethnicity) may alter the ways in which genes and environment influence health. In this article, we use natural experiments involved in twin births to help untangle how genetic and prenatal environmental variation contribute to associations between birth weight and infant mortality among white and black infants in the United States.

White—black differences in infant health in the U.S. provide a useful focus for exploring the intersection between genes, environmental exposures, and health disparities. Black singleton babies in the U.S. are about twice as likely as white singleton babies to be born low birth weight and die during the first year of life (NCHS, 2010). While social and economic disadvantages clearly contribute to poorer infant health among black Americans, selected empirical patterns (e.g., apparent paradoxes in birth weight-specific survival curves) have repeatedly raised questions about potential “inherent” tendencies toward different “optimal” sizes at birth across race, as well as proposals for race-specific medical thresholds for birth weight (Vangen et al., 2002; Wilcox & Russell, 1990).

The following analysis, which attempts to identify potential gene—environment interactions contributing to race disparities in infant health, faces methodological identification challenges that are common in research addressing questions of “nature” and “nurture.” Genetic and environmental variation often co-vary and limitations in most existing datasets make it extremely difficult to observe whether individuals with particular health outcomes share genetic compositions and/or environmental exposures. In this analysis, we attempt to surmount these challenges by exploiting two “natural experiments” that arise with twin pregnancies. Our first strategy focuses on prenatal environmental variation within twin pairs. Within a given twin pregnancy, differences in fetal positions in utero generate random variation in prenatal environmental inputs (e.g., nutrients, oxygen). To capture this within-womb variation in environmental inputs, we use twin fixed effects estimation. Our second natural experimental strategy isolates genetic variation within twin pairs by comparing identical and fraternal twin estimates. Because identical twins share 100 percent of their genotype, while fraternals share only about 50 percent, comparing our fixed effects estimates across identical and fraternal twins allows us to assess whether within-pair differences in prenatal environmental inputs (i.e. womb position) have varying effects on infant mortality in the presence or absence of genetic variation within the twin pair. Stratifying the identical and fraternal fixed effects estimates by race allows us to further explore whether these sources of genetic and environmental variation may have differing consequences for white and black twin pairs. Data for
the analysis come from the 1997 Matched Multiple Birth Dataset. As with most existing national datasets, these data do not allow us to directly observe twins’ zygosity. However, we overcome this data limitation by imputing estimates for the population of identical twin pairs. Our imputation strategy draws on Weinberg’s (1902) assumptions about identical twinning rates and twin pair sex composition. In the following models, birth weight—mortality associations are similar for white identical and fraternal twins. However, birth weight—mortality associations are notably stronger for black identical twins, relative to black fraternal twins. Such differences across the white and black estimates provide suggestive evidence that genetic and environmental inputs into infant health may vary across race groups in the U.S. In our interpretation, we consider multiple potential explanations for these results (e.g., disparities in post-natal resources and health care, potential population genetic variation, etc.). Trying to concretely interpret these group differences in terms of alternative potential underlying mechanisms, however, raises several additional questions and ultimately highlights the complexities involved in trying to untangle the intersection of genes, environmental exposures, and health disparities.

Conceptual issues and controversies related to genes, environmental inputs, and health disparities

Genetic and environmental inputs may have varying influences on health across more or less favorable circumstances (Lewontin, 2000). As an example, it is well-recognized that individuals may not reach their genetic potential for body size (e.g., height and weight) without proper nutrition. Nutritional inputs may also offer differential returns for helping people reach their genetic potential for growth if groups in a population face different rates of additional adversities (e.g., psychosocial traumas or childhood infections, which may hinder growth; Deaton, 2007). Considering the transmission of genes across multiple generations, selection pressures and patterns of assortative pairing shaped by geographic and social boundaries may also determine which particular genes associated with growth and size are passed on to future generations within groups and populations. In sum, the interactive effects of genes and environment may differ across broader circumstances, and it is conceivable that the influences of genetic and environmental inputs into health may vary across groups facing different levels of advantage and adversity within society.

However, trying to actually investigate such possibilities with a concrete case, such as race disparities in infant health in the U.S., raises many complexities and controversies. Although geographic boundaries (e.g., continental divides) and social systems of stratification (e.g., laws prohibiting intermarriage), could conceivably create assortative pairing patterns that generate meaningful genotypic differences by ancestry/race, many authors argue that race does not have real biological/genetic meaning. For instance, citing much greater genetic variation within rather than between racial groups, authors, have argued that race categories are not meaningful genetic groupings, and rather reflect social taxonomies (Braun, 2002).

In this analysis, we treat race categories as social constructions, and understand genetically-related explanations of health disparities to be rooted in historical and social structural conditions (e.g., the “robustness” hypotheses discussed below reflect biological adaptations to conditions of social inequality). However, considering genetic influences on health disparities at all (even with significant attention to social factors) raises a number of concerns, particularly regarding potential policy implications. A long history of dubious scientific work has used genetic and biological explanations for race disparities to motivate and justify discriminatory practices (Stephan & Gilman, 1991). At this point in history, technologies that allow for genetically-targeted medicine renew concerns that genetic explanations for health outcomes may intersect with socially-constructed racial inequalities to create new, potentially unethical, linkages between race, genetic information, and medical practice (Duster, 2003). On the other hand, in spite of these real concerns, some take the alternative view that it would be wrong to not consider possible racial differences in genetic determinants of health if there is potential for certain race or ethnic groups to benefit from more genetically-targeted treatments (for review of relevant debates see Braun, 2002).

In spite of these controversies, and the methodological complexities discussed below, large white—black disparities in infant health—combined with multiple published proposals for race-specific birth weight standards in medicine (e.g., Vangen et al., 2002; Wilcox & Russell, 1990) —make it seem highly worthwhile to investigate gene—environment intersections with regard to race differences in birth weight and infant mortality.

Genetic and environmental determinants of birth weight

Birth weight is an important indicator for newborns’ health and viability. Relative to their larger counterparts, babies born with low birth weight (<5.5 pounds) face much higher risks of infant mortality and poor childhood health, and they typically obtain less education and earn less as adults (Behrman & Rosenzweig, 2004; Bennett, 1997; NCHS, 2010). Variations in birth weight are likely to reflect both genetic and environmental determinants. Evidence shows that environmental stressors, including famines (Lumey, 1992), air pollution (Currie & Walker, 2009), and even unemployment rates (Catalano, Hans-Tore, & Hartig, 1999), can lower birth weight. Studies comparing the offspring of identical and fraternal twins have estimated that 40–60% of the variation in birth weight may be genetically determined although, these estimates may be upwardly biased because of unmeasured correlations between twins’ genetic and environmental similarities (Clausson, Paul, & Cnattingius, 2000; Magnus, Berg, Bjerkedal, & Nance, 1984). Recent studies using genome scan technologies present evidence of correlations between birth weight and particular genetic markers [although interactions between multiple polymorphisms may confound these estimates (Infante-Rivard, 2010)]. While both genes and environmental inputs likely matter to birth weight and infant mortality, the relative contributions of these factors may differ when fetuses face additional constraints (e.g., insufficient time to grow because of premature birth). Examining birth weight—mortality associations for identical and fraternal twins with varying gestational ages, Conley, Strully, and Bennett (2006) found that, in preterm pregnancies that lasted less than 37 weeks, associations between birth weight and infant mortality were similar for identical and fraternal twins, suggesting that environmental variation could account for birth weight effects in premature twin births. However, in full-term pregnancies, underlying genetic variation appeared to generate larger birth weight—mortality associations for mature fraternal twins, relative to mature identical twins. The authors suggest that, when twins had ample time in which to grow, but were still born severely growth retarded, underlying genetic vulnerabilities may be more likely to drive mortality risk. The following analysis uses a similar strategy to Conley et al. (2006) but compares across race groups rather than gestational age.

Genes, environmental inputs, and race disparities in infant health

There are clear social and economic disadvantages experienced by black Americans (e.g., poverty, segregation, and discrimination)
which certainly contribute to lower birth weights among black babies (Williams & Collins, 1995). However, in seeming contrast to such socioeconomic explanations, are select empirical patterns which appear to point to “inherent” tendencies toward race differences in “optimal” sizes at birth. Black singleton babies tend to be born smaller than white babies, regardless of gestational age, and some authors examining distinct causes of infant death hypothesize that black fetuses may be more physiologically mature than white fetuses in the earlier weeks of gestation (Alexander, Tompkins, Altekruse, & Hornung, 1985). While both low birth weight and infant mortality are more common among black babies than white babies, a black baby born low —birth weight is more likely to survive than a white baby born at a similar weight (Wilcox & Russell, 1990). Some authors have interpreted this apparent “survival paradox” as suggesting that lower birth weights may be advantageous, or at least less harmful, for black babies than white babies. After showing that birth weight, expressed relative to a race–ethnicity specific standard, rather than an overall population standard, is a better predictor of mortality, Wilcox and Russell (1990) and Vangen et al. (2002) have argued in favor of race–ethnicity specific standards to evaluate birth weight and medical risk (i.e. they argue that the cut-off for a medically-risky birth weight should perhaps be lower for black babies than white babies). Without a clearer understanding of what actually drives race differences in birth weight and mortality, such proposals for changes to medical policy/practice seem at risk of playing into overly-simplistic, biologically-deterministic views of racial health disparities.

Integrating the above empirical patterns (e.g., survival paradox) with social stratification perspectives, some authors raise the possibility that black babies’ smaller sizes may reflect a biological and/or genetic adaptation to adverse social and environmental circumstances (i.e., the “robustness hypothesis”) (Mangold & Powell-Griner, 1991; North & MacDonald, 1977). Given adverse conditions, a smaller size may be an advantage. With inadequate environmental resources, giving more energy to organ development, and less to overall body size, is likely to increase survival. In an evolutionary adaptive scenario, genetic mutation and natural selection over generations could have led black babies to have more “thrifty genotypes” that are better suited to environmental deprivation. In an individual-level gene-expression scenario, disproportionate exposure to prenatal environmental stressors among black fetuses could lead to a “thrifty adaptive response,” altering how genotypes for growth and development are expressed.

**Analytic strategy: within-twin estimates stratified by race and sex composition/zygosity**

Our analytic strategy builds on two “natural experiments” that arise from the unique biology of twin pregnancies. First, within a given twin pregnancy, differences in fetus’s positions generate essentially random variation in prenatal environmental inputs. Differences in uterine vascular density and architecture mean that one twin often receives more nutrients, oxygen, and protective hormones than the other, and is frequently born larger than his/her co-twin (Hall, 2003). Second, we exploit genetic differences across identical and fraternal twins. The splitting of a fertilized egg creates identical twins who share 100 percent of their genotypes; whereas, the fertilization of multiple eggs creates fraternal twins who share about 50 percent of their genotypes.

Our analysis employs within-twin (i.e., fixed effects) regression models. For the total sample and each race group, we generate within-twin estimates stratified by either the pair’s sex composition or zygosity (using the Weinberg assumption to obtain imputed identical twin estimates). Pair sex composition can be seen as crude proxy for zygosity because all different-sex twins are necessarily fraternal, while same-sex twins will be a combination of identical and fraternal. Our interpretation focuses on comparing within-twin estimates across a series of models stratified by race, sex composition, and zygosity. Here, we discuss the key features and assumptions of our analytic strategy and methods.

**Within-twin comparisons using Fixed Effects (FE) models**

Our results are based on linear probability twin FE models, which can be written as,

\[
Y_{ij} = \beta_0 + \beta_1 BW_{ij} + \beta_2 X_{ij} + \nu_j + \epsilon_i
\]

where \( i \) refers to the first or second twin in the \( j \)-th twin set, \( Y_{ij} \) indicates whether the \( i \)-th twin in the pair died, \( BW_{ij} \) indicates the birth weight of the \( i \)-th twin in the pair, and \( X_{ij} \) indicates a set of individual-level controls for the \( i \)-th twin (e.g., first born, female). \( \nu_j \) refers to twin pair-level unobserved characteristics, and \( \epsilon_i \) refers to individual-level unobserved characteristics. The key feature of these models is that they capture variation within twin pairs, while holding constant any factors that do not vary within the twin pair. Equation (1) is a linear probability model—i.e., a linear, OLS model with a dummy dependent variable. Coefficients based on this equation can be interpreted as percentage changes in the probability of death for a twin within a given pair (i.e., relative to the other twin in the set).

When interpreting the twin FE estimates, two key points should be kept in mind. First, because twins are born at virtually the same time, gestational age will not vary within pairs and birth weight differences within pairs will be the result of growth restriction. This etiological specificity will make interpretation of the results more straightforward. Second, because twins share the same pregnancy, any unmeasured factors that do not vary within pregnancies—including potential confounders—are held constant. Comparing across pregnancies (e.g., singleton births), prenatal environments will likely reflect several endogenous factors including maternal behaviors and circumstances. However, within pregnancies (e.g., within twin pairs), such factors are held constant and environmental variation reflects different positions within the womb, which result from the exogenous process of implantation within the uterus.

**Identical and fraternal twin comparisons**

To consider questions of “nature” and “nurture,” we present separate FE estimate for identical and fraternal twin pairs (employing the Weinberg assumption to impute estimates for identical twins). Within identical pairs, genetic variation will be held constant, and birth weight differences will be driven entirely by variation in prenatal environment (i.e., womb position). Within fraternal pairs, genetic factors will vary, and birth weight differences will reflect a combination of genetics and prenatal environment. Finding different associations for identical and fraternal twins would then suggest that environmental and genetic inputs into birth weight have different consequences for infant health. The biggest potential confounder for the comparisons by zygosity arises from correlations between genetic variation and placental formation. Virtually all fraternal twins are dichorionic—meaning that they each have their own placenta. The majority of identical twins (70–75 percent), however, are monochorionic—meaning that they share a placenta (Hall, 2003). Being monochorionic typically causes more unequal sharing of the placenta and nutrition within the twin pair. If low birth weight resulting from environmental competition within twin pairs is more hazardous than low birth weight resulting from genetic
causes, our identical twin estimates may be overestimated. This will be kept in mind when interpreting the results. However, we know of no reason that the relationship between zygosity and placental formation should vary by race. That is, to the extent that chromionicity may confound our identical—fraternal comparisons, we expect that bias should operate the same for white and black twins, implying that differences by race are unlikely to be biased by chromionicity.

Imputing identical twin coefficients using the Weinberg assumption

The Matched Multiple Birth Dataset that we use in this analysis is an American national-level dataset. However, like most national birth datasets, it does not have information on twins’ zygosity. Therefore, we rely on certain assumptions about sex compositions and twinning rates to impute birth weight—mortality associations for identical twins.

Our first step in considering zygosity is simply to stratify according to pairs’ sex composition. Different-sex twins (i.e., a male and female pair) must be fraternal, while same-sex twins (i.e., two males or two females) may be either identical or fraternal. Estimates based on same-sex pairs (some proportion of which will be identical) should, therefore, contain less genetic variation than estimates based on different-sex pairs (who are all fraternal).

Next, to drill down further and obtain a clearer estimate for the identical pairs within the population of same-sex twins, we employ an imputation strategy based on the Weinberg assumption. In 1902, Weinberg argued that one may use the sex ratio of a twin population to estimate the number of identical twins in the population. To illustrate the logic of the Weinberg assumption with a simple example, assume that twins are equally likely to be male as to be female. In this simple demonstration with a sex ratio of 100, the number of opposite-sex twins—who are all necessarily fraternal—should equal the number of fraternal same-sex twins. To isolate the identical twins in the same-sex twin group one could then subtract the number of opposite-sex twins from the number of same-sex twins. Borrowing a simple example from Conney and Mackey (1996), with 100 twin pairs, 30 of which were opposite-sex and 70 of which were same-sex, we would assume that 30 of the same-sex pairs were fraternal and, consequently, 40 of the same-sex pairs were identical. The Weinberg assumption has performed reasonably well in validity tests in recent decades (for a review of these tests see the online supplemental materials). In the following analysis, we present a robustness test to assess the sensitivity of our imputed results to violations of the Weinberg assumption.

We use this sex ratio-based estimate of the proportion of same-sex twins that are identical to impute coefficients for the identical twin population. After running models stratified according to pair sex composition, we use the following weighted average strategy to impute estimates for identical pairs within the population of same-sex twins. If:

- \( a \) = effect of birth weight for the mixed-sex group (who must all be fraternal)
- \( b \) = effect of birth weight for identicals (unknown entity)
- \( c \) = effect of birth weight for the same-sex group (which is a combination of identicals and fraternals), and
- \( p \) = the sex ratio of the population; i.e., the proportion female (based on the Weinberg assumption, this will equal the fraction of identical twins in the same-sex group),

then we can treat \( c \) as a weighted average of \( a \) and \( b \):

\[
c = bp + a(1 - p)
\]  

Here, the coefficient for the same-sex group, \( c \), is treated as the sum of:

(i) \( b \), the unknown coefficient for the identical twins, weighted by \( p \), the proportion female in the population (which should be equivalent to the fraction of identical twins in the same-sex group); and

(ii) \( a \), the coefficient for the different-sex pairs (which are all fraternal), weighted by the proportion of male twins (i.e., 1 minus the proportion of females).

Since we know \( c \), \( a \), and \( p \), we can solve for the coefficient for identical twins, \( b \):

\[
b = \frac{c - a(1 - p)}{p}.
\]  

For an explanation of standard errors for the imputed twin estimates see the online supplemental materials.

In essence, this imputation strategy treats a coefficient for our same sex subsample as an average of the effects for both identical and fraternal twins, and then uses this observed coefficient to solve for a separate identical twin estimate, according to Weinberg (1902) that the proportion of identical twins in the same-sex group is equivalent to the proportion female in the total twin population. The key assumption underlying this strategy is relative consistency in birth weight effects and rates of identical twinning across sex composition. For instance, our imputations could be compromised if there are interactions between birth weight differences within pairs and the gender composition of pairs, net of zygosity. We cannot test for such an interaction with our data since we cannot observe zygosity. There is some evidence (based on a few small samples) of excess mortality among same-sex male fraternal twins; however, this excess appears to be limited to cases in which both twins died (Boklage, 1985; Myrianthopoulos, 1970). Since our FE estimates are based entirely on discordance within the twin pair, such a pattern should not pose too large a concern for our analysis.

Our imputations might also be inaccurate if identical and fraternal twinning is associated with the sex composition of pairs. Our imputation strategy does not require that identical or fraternal twinning be purely randomly distributed across the population. However, it does require that the likelihood of twinning not be associated with the sex composition of pairs. For instance, increased use of artificial reproductive technology (ART), has clearly increased rates of fraternal twinning, and may also have increased rates of identical twinning, in recent decades (Martin & Park, 1999; Platt, Marshall, & Pharoah, 2001). However, this should not compromise our imputation strategy, unless ART has also affected the likelihood that identical or fraternal twins have particular sex compositions (e.g., increasing the likelihood of same-sex over different-sex pairs), which seems relatively unlikely. It is also worth clarifying that, because we are using FE models, ART-use, and factors associated with ART-use (e.g., education, age, etc.), will only bias our race-specific estimates if they contribute to birth weight and mortality discordance within twin sets. Any risks associated with ART-use that are shared by both twins in a set will be factored out of the race-specific FE estimates.

We use the observed race-specific values for proportion female to impute separate identical twin estimates for the white and black populations. This means we do not need to assume that identical or fraternal twinning rates are consistent across race groups in the U.S. There is evidence that twinning rates vary by race in the U.S., and more common use of ART has increased fraternal twinning more among whites than blacks (Hall, 2003; Oleszczuk, Cervantes, Keith, & Keith, 2001). However, these types of race differences in twinning
rates should not comprise our imputations, unless these factors are also associated with the sex composition of twin pairs. As an example, if whites were more likely than blacks to have pairs of female identical twins, rather than male identical twins (or vice versa), this could compromise the use of the weighted average strategy by race groups. However, a difference in twinning by race that is not sex-specific in this way should not comprise the imputed estimates.

Finally, for the coefficient for the same-sex sample to be an accurate weighted average of effects for identical and fraternal twins, the variance of birth weight must be the same across both groups. Since we cannot observe zygosity in our data, we cannot directly test this. Examination of our data suggests that the variance in individual twins’ birth weights is slightly larger in the same-sex pairs, whereas the variance in within-pair birth weight discordance is slightly smaller in the same-sex pairs (results not shown). Given such differences, the precise point estimates we impute for identical twins must be interpreted with some caution.

Comparing estimates across white and black twins

To address our larger research question of whether genetic and prenatal environmental inputs differ across race categories in the U.S., we run separate models for white and black subsamples. We then test for statistically significant differences across the race-specific birth weight coefficients using $z = (b_1 - b_2) / \sqrt{(s_1^2 + s_2^2)}$ (Clogg, Petkova, & Haritou, 1995). In each race-specific model below, the twin FE estimates can be interpreted in a typical fashion (i.e., as within-twin pair variation). When comparing the FE estimates across race (e.g., comparing estimates across the white model and the black model), we are considering how within-twin pair variations (e.g., birth weight discordance) differ across race groups. Any race differences across the within-twin estimates are likely to reflect broader, “upstream” social and environmental issues. Because race is a critical dimension of social stratification in the U.S., many different components of resources, living conditions, and well-being differ by race and may play a role in infant health. As we discuss further below, potential race-related factors that seem most relevant to our results include disparities in neonatal health care, broader socioeconomic inequality, and differential use of ART.

Sample and variables

The 1995–1997 Matched Multiple Birth Dataset, published by the National Center for Health Statistics, was created by combining the U.S. Live Birth and Fetal Death files with the Linked Live Birth/Infant Death Cohort Datasets [Martin, Curtin, Saulnier, & Mousavi, 1998]. These data are based on Vital Statistics and contain virtually all multiple births in the selected years.

We restrict our analysis to preterm twins. The stress of a multiple gestation pregnancy means that most twins are born prematurely, and, after about 39 weeks, infant mortality rates actually begin to increase with gestation (Hall, 2003; Cheung et al., 1995). Results from Conley et al. (2006) further suggest that low birth weight, mature twins are a particularly vulnerable subgroup. Restricting our sample to pairs of preterm twins who were both born alive and who both have valid information on all of the variables in our analysis yields 138,010 individual twins (69,005 pairs). The white subsample contains 77,306 individual twins (38,653 pairs), and the black subsample contains 15,208 individual twins (7,640 pairs). The mean gestational age in the sample is 33.3 weeks, and this is consistent across the white and black samples. For descriptive statistics, stratified by race, see Table 1. The average twin in this sample weighs about 4.6 pounds and faces a 4.5 percent chance of infant mortality. Birth weights and the risk of infant mortality do not appear to vary across the white and black samples. This secondary analysis of administrative data (with no identifying information) was granted human subjects exemption status.

Variables

**Birth weight**, measured in pounds, is specified with a piecewise linear spline with nodes at 3.3 pounds and 5.5 pounds. This specification, which aligns with standard medical thresholds of “very low birth weight” and “low birth weight,” accounts for non-linear relationships between birth weight and mortality, and estimates survival within three different birth weight ranges (i.e., <3.3 lbs, 3.3–5.5 lbs, and >5.5 lbs).

**Infant mortality** is a dichotomous outcome coded one if a twin died under one year of age.

Control variables include dichotomous indicators for whether a twin was **first born** or **female**.

Results

Table 2 presents the FE models, stratified by sex compositions. First, we can note the quickly diminishing returns to birth weight. Considering the first column containing a model for all pairs (i.e., regardless of race or sex composition), a one-pound increase in the very low birth weight range (1st segment, < = 3.3 pounds) reduces a twin’s risk of death (relative to the other twin in the set) by almost 10 percentage points. However, a similar one-pound increase in the low birth weight range (2nd segment, > 3.3, < = 5.5 pounds) or the normal birth weight range (3rd segment, > 5.5 pounds) reduces the risk of death within the twin set by less than one percentage point.

Focusing on the more notable estimates found within the 1st segment range, we can look down Table 2 to compare across race. Comparing across the white and black models in the first column, a one-pound increase in 1st segment range reduces the risk of mortality for a white twin within a given pair by 9.2 percentage points and for a black twin by 8.5 percentage points. The mortality reduction in the white sample is slightly larger than in the black sample, but this difference is not statistically significant at the .05 level.

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**Table 1**

<table>
<thead>
<tr>
<th>Sample means, by race</th>
<th>Total (N = 138,010)</th>
<th>White (N = 77,306)</th>
<th>Black (N = 15,280)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant mortality</td>
<td>.046</td>
<td>.046</td>
<td>.045</td>
</tr>
<tr>
<td>(208)</td>
<td>(.096)</td>
<td>(.096)</td>
<td>(.096)</td>
</tr>
<tr>
<td>Birth weight (pounds)</td>
<td>4.615</td>
<td>4.620</td>
<td>4.599</td>
</tr>
<tr>
<td>(1.429)</td>
<td>(.398)</td>
<td>(.398)</td>
<td>(.396)</td>
</tr>
<tr>
<td>First segment</td>
<td>3.112</td>
<td>3.113</td>
<td>3.110</td>
</tr>
<tr>
<td>(&lt; = 3.3 pounds)</td>
<td>(.110)</td>
<td>(.110)</td>
<td>(.110)</td>
</tr>
<tr>
<td>Second segment</td>
<td>1.317</td>
<td>1.321</td>
<td>1.304</td>
</tr>
<tr>
<td>(&gt; = 3.3, &lt; = 5.5 pounds)</td>
<td>(.844)</td>
<td>(.843)</td>
<td>(.845)</td>
</tr>
<tr>
<td>Third segment</td>
<td>.186</td>
<td>.186</td>
<td>.185</td>
</tr>
<tr>
<td>(&gt; = 5.5 pounds)</td>
<td>(.198)</td>
<td>(.198)</td>
<td>(.195)</td>
</tr>
<tr>
<td>First born</td>
<td>.500</td>
<td>.500</td>
<td>.500</td>
</tr>
<tr>
<td>female</td>
<td>.490</td>
<td>.491</td>
<td>.485</td>
</tr>
<tr>
<td>(283)</td>
<td>(.096)</td>
<td>(.096)</td>
<td>(.096)</td>
</tr>
</tbody>
</table>

* Standard deviations in parentheses, within-pair standard deviations in brackets.
Comparing the results in columns 2 and 3 for the different-sex and same-sex pairs, we can begin to indirectly consider questions about zygosity and genetic and environmental determinants. Recall that the different-sex sample will be all fraternal, while the same-sex sample will be a combination of identical and fraternal. Beginning with the total sample at the top of Table 2, we see that, in the second column, a one-pound increase in the 1st segment range is associated with a 10 percentage point reduction in the risk of mortality. In the third column, a similar one-pound increase within a same-sex twin pair is associated with about a 10 percentage point reduction in the risk of mortality. In the second column, a one-pound increase within a same-sex twin pair is associated with an extra 10 percentage point reduction in risk. For one twin, relative to the other. Within a same-sex, black twin pair, however, an equivalent one-pound increase is associated with a larger and statistically significant 10 percentage point reduction in risk for one twin, relative to the other. These comparisons across sex compositions provide preliminary evidence that birth weight–mortality associations may be larger among black identical twins than black fraternal twins.

Moving onto Table 3, we can test these preliminary findings with our imputed identical twin estimates. As explained above, the

### Table 3

<table>
<thead>
<tr>
<th>Total sample</th>
<th>Fraternals (different-sex)</th>
<th>Indenticals (imputed)</th>
<th>Signif. of Difference</th>
<th>White sample</th>
<th>Fraternals (different-sex)</th>
<th>Indenticals (imputed)</th>
<th>Signif. of difference</th>
<th>Black sample</th>
<th>Fraternals (different-sex)</th>
<th>Indenticals (imputed)</th>
<th>Signif. of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st segment (&lt;3.3 lbs)</td>
<td>.097*** (.003)</td>
<td>.116*** (.010)</td>
<td>**</td>
<td>1st segment (&lt;3.3 lbs)</td>
<td>.095*** (.008)</td>
<td>.085*** (.013)</td>
<td>ns</td>
<td>.034 (.019)</td>
<td>.180*** (.031)</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>2nd segment (&gt;3.3, &lt;5.5 lbs)</td>
<td>.004*** (.001)</td>
<td>.005 (.004)</td>
<td>ns</td>
<td>2nd segment (&gt;3.3, &lt;5.5 lbs)</td>
<td>.004 (.003)</td>
<td>.006 (.005)</td>
<td>ns</td>
<td>.013 (.007)</td>
<td>.023*** (.012)</td>
<td>***</td>
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</tr>
<tr>
<td>3rd segment (&gt;5.5 lbs)</td>
<td>.006 (.003)</td>
<td>.005 (.005)</td>
<td>ns</td>
<td>3rd segment (&gt;5.5 lbs)</td>
<td>.008 (.004)</td>
<td>.002 (.007)</td>
<td>ns</td>
<td>.005 (.009)</td>
<td>.003 (.017)</td>
<td>ns</td>
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</tr>
</tbody>
</table>

a Fraternal estimates are based on twin fixed effects coefficients for the different-sex sample (see column 2 in Table 2); Identical estimates are based on imputation. Standard errors in parentheses.

b Statistical tests for differences in coefficients were calculated using $z = (b_1 - b_2) / \sqrt{(se_1)^2 + (se_2)^2}$ (Clogg et al., 1995).

c Using the formula in note 2, we detected the following statistically significant differences in birth weight coefficients across the white and black models: For the fraternal (i.e., different-sex) twins, the first segment birth weight estimate is statistically significantly different at the .05 level. For the identical (imputed) twins, the first segment birth weight estimate is statistically significantly different at the .05 level. All other birth weight coefficients are statistically equivalent across the white and black models.

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fraternal estimates are based on the point estimates for the observed different-sex sample (i.e., the fraternal estimates in Table 3 are equivalent to the different-sex birth weight results in column 2 of Table 2). The identical twin estimates, on the other hand, are generated based on our imputation strategy. Overall, the differences between the fraternal (i.e., mixed sex) and identical (i.e., imputed) estimates conform to the patterns revealed by the sex composition comparisons. Looking at the 1st segment estimates for the total sample, the imputed estimate for identical twins is slightly larger than the estimate for fraternal twins. Breaking the models down by race, this difference is more pronounced within the black sample. There is no significant difference between the identical and fraternal estimates within the white sample; they both reflect about a nine percentage point reduction in risk. But, within the black sample, the imputed identical estimate is large and significant, while the fraternal estimate is small and insignificant. A one-pound increase in the very low birth weight range is associated with a large 18 percentage point reduction in a black identical twin’s risk of infant mortality, relative to the other twin in the pair. But, for a black fraternal twin, an equivalent one-pound increase is associated with a statistically insignificant three percentage point reduction in risk.

Robustness test of imputed identical estimates

As outlined previously, our imputation strategy required several assumptions and could be limited in multiple ways. Most notably, the Weinberg assumption may not be valid if, p, the proportion female in the twin population, does not equal the number of same-sex twins that are identical (see Eq. (3), above). As a robustness test of how the results would change if the Weinberg assumption were off and the fraction of identical twins were accurately modest. Most importantly, when comparing these alternative imputed twin estimates to the equivalent mixed-sex (i.e., fraternal) estimates, there are no changes in the results of the tests for significant differences across coefficients. Even with alternative values for p, we still find that, for the 1st segment estimates, birth weight—mortality associations among black identical twins are significantly larger than among black fraternal. However, among white twins, there are still no significant differences in identical and fraternal estimates. Our main findings are robust when we relax the Weinberg assumption and allow the twin sex ratio to vary by up to 10% (which is a substantial change in a population sex ratio).

When evaluating sensitivity to violations of the Weinberg assumption, it is also notable that we find consistent results for the mixed- and same-sex estimates in Table 2 and for the fraternal and imputed identical estimates in Table 3. As stated above, sex composition provides a rough indicator of zygosity since all mixed-sex twins must be fraternal, while the same-sex twins may be either identical or fraternal. Overall, results of the robustness test presented in Table 4 and consistent findings across the imputed and sex-stratified estimates suggests that our findings regarding race differences in birth weight—mortality associations among identical and fraternal twins do not depend on the particularities of the Weinberg assumption and/or our imputations.

Table 4

Imputed birth weight coefficients for identical twins using a range of values for proportion female (p).

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(obs value = .10)</td>
<td>(obs value = .05)</td>
<td>(obs value = .05)</td>
<td>(obs value = .05)</td>
<td>(obs value = .10)</td>
</tr>
<tr>
<td>Total sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st segment*</td>
<td>−.123*** (.014)</td>
<td>−.119*** (.012)</td>
<td>−.116*** (.010)</td>
<td>−.113*** (.009)</td>
<td>−.111*** (.008)</td>
</tr>
<tr>
<td>2nd segment*</td>
<td>−.004 (.006)</td>
<td>−.005 (.005)</td>
<td>−.005 (.004)</td>
<td>−.005 (.004)</td>
<td>−.005 (.004)</td>
</tr>
<tr>
<td>3rd segment*</td>
<td>.002 (.007)</td>
<td>.001 (.006)</td>
<td>.000 (.005)</td>
<td>.000 (.005)</td>
<td>.001 (.004)</td>
</tr>
<tr>
<td>White sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st segment*</td>
<td>.082*** (.018)</td>
<td>.084*** (.015)</td>
<td>.085*** (.013)</td>
<td>.086*** (.011)</td>
<td>.087*** (.010)</td>
</tr>
<tr>
<td>2nd segment*</td>
<td>−.006 (.007)</td>
<td>−.006 (.006)</td>
<td>−.006 (.005)</td>
<td>−.006 (.004)</td>
<td>−.006 (.004)</td>
</tr>
<tr>
<td>3rd segment*</td>
<td>.005 (.010)</td>
<td>.003 (.008)</td>
<td>.002 (.007)</td>
<td>.001 (.007)</td>
<td>.000 (.006)</td>
</tr>
<tr>
<td>Black sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st segment*</td>
<td>−.218*** (.043)</td>
<td>−.197*** (.037)</td>
<td>−.180*** (.031)</td>
<td>−.167*** (.028)</td>
<td>−.155*** (.024)</td>
</tr>
<tr>
<td>2nd segment*</td>
<td>−.029 (.017)</td>
<td>−.027 (.015)</td>
<td>−.025 (.012)</td>
<td>−.024 (.011)</td>
<td>−.023 (.010)</td>
</tr>
<tr>
<td>3rd segment*</td>
<td>−.005 (.023)</td>
<td>−.004 (.020)</td>
<td>−.003 (.017)</td>
<td>−.002 (.015)</td>
<td>−.002 (.014)</td>
</tr>
</tbody>
</table>

* All the imputed twin estimates in this row are significantly different at .05 level from the equivalent mixed-sex (i.e., fraternal) estimates.

b None of the imputed twin estimates in this row are significantly different at .05 level from the equivalent mixed sex (i.e., fraternal) estimates.

Conclusion

Summarizing the 1st segment results in Table 3, the estimates for white identical and fraternal twins were very similar. However, within the black sample, the estimate for identical twins was large and significant, while the estimate for fraternal twins was small and insignificant. Estimates based on fraternal twins were also never significantly larger than the imputed identical twin estimates, suggesting that, regardless of race, prenatal environmental variation can account for at least part of the birth weight—mortality associations among identical and fraternal twins do not depend on the particularities of the Weinberg assumption and/or our imputations.
are suffering more from the biological complexity of shared placentas and identical twinning. More adverse socioeconomic conditions among black mothers may mean that the greater within-uterine environmental competition experienced by all identical twins is more consequential for black identical twins. Alternately, racial disparities in neonatal care might create greater mortality elasticity among identical twins who are already at an at-risk population. Considering genetic explanations, one could imagine that this pattern reflects greater genetic vulnerability to prenatal environmental stressors among black fetuses. However, this seems unlikely because it contradicts the prevailing “robustness” hypothesis in which higher birth weight–specific survival rates among black singleton babies are seen as reflecting adaptation to harsh environmental conditions.

Interpreting potential underlying mechanisms becomes increasingly complicated if we focus on the race differences across the fraternal estimates. We find that higher birth weights reduce white fraternal twins’ mortality risk, but appear to have no effect for black fraternal twins. While fraternal twins may experience less environmental competition and medical complications than their identical counterparts, they still experience a notable amount. So, if, say, socioeconomic adversity or disparities in neonatal care were driving the larger effects among black, relative to white, identical twins, we would expect to see slightly different estimates among black fraternal, relative to white fraternal, twins. Since fraternal twins face genetic variation that is not an issue for the identical twins, smaller effects among black, relative to white fraternal twins, could be interpreted as evidence that genetic differences among blacks mitigate the environmental effects of womb position (i.e., support for the “robustness” hypothesis). However, such a gene-based explanation seems unlikely, particularly since it would be directly contradicted by the pattern of the identical twin estimates. A final possibility has to do with the use of ART. If the effect of birth weight is negligible for fraternal twins that are spontaneous, but matters in those pairs that result from ART, then racial differences could result from the higher prevalence of ART among whites. This is, however, pure speculation and would require a direct test of the birth weight–mortality relationship across ART versus spontaneous twinning.

The unique biology that generates natural experimental variation within twin pairs may limit how far we can generalize our results to singleton populations. Since most twins are born low birth weight and preterm, estimates based on twins extend most directly to smaller, preterm singletons. Twin FE estimates, in which gestational length determined by studies of offspring of twins. Accordingly, these results may shed light on racial disparities among smaller singleton babies that are associated with growth restriction, but not necessarily on disparities associated with differences in gestational age. The twin data for this analysis also do not reveal substantial race differences in birth weight or infant mortality. This may suggest that the unique biology of twinning suppresses race disparities in risk typically seen in singleton populations. However, it remains reasonable that race differences in mechanisms underlying birth weight and survival do not necessarily differ for singleton and twin births—most notably, any possible population-level differences in genetic tendencies by race would seem very unlikely to differ among parents having twin versus singleton births. With increases in multiple births, understanding the sequelae of low birth weight among this population—and any attendant racial differences in those consequences—will only grow in importance over the foreseeable future.

Research into health disparities must move beyond overly-simplistic questions about whether genes or environments matter for health to consider how genetic and environmental inputs into health may differ across varying circumstances or populations. However, as evidenced by the multiple interpretations outlined above, trying to identify the precise mechanisms driving group differences may also run up against the reality of complex relationships between genes, environment, and social stratification. Our finding of stronger birth weight–mortality associations among black identical twins, relative to white identical twins, is particularly intriguing, and may point to interactions between within-uterine twin competition and larger social and environmental inequities by race in the U.S.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.socscimed.2012.09.024.

References


Braun, L. (2002). Race, ethnicity, and health: can genetics explain disparities? Perspectives in Biology and Medicine, 45(2), 139–150.


