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EPIDEMIOLOGY

Vanishing twins, spared cohorts, and the birthweight of periviable infants born to Black and white women in the United States

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Pregnancies ending before 26 weeks contribute 1% of births but 40% of infant deaths in the United States. The rate of these “periviable” births to non-Hispanic (NH) Black women exceeds four times that for NH whites. Small male periviable infants remain most likely to die. NH white periviable males weigh more than their NH Black counterparts. We argue that male infants born from twin gestations, in which one fetus died in utero (i.e., the vanishing twin syndrome), contribute to the disparity. We cannot directly test our argument because “vanishing” typically occurs before clinical recognition of pregnancy. We, however, describe and find associations that would emerge in vital statistics were our argument correct. Among male periviable singleton births from 288 monthly conception cohorts (January 1995 through December 2018), we found an average NH white advantage of 30 grams (759 grams versus 729 grams). Consistent with our argument, however, cohorts signaling relatively few survivors of the vanishing twin syndrome showed no disparity.

INTRODUCTION

Infants born before completing 26 weeks of gestation account for less than 1% of live births in the United States but more than 40% of infant deaths (1). The rate of these “periviable” births to non-Hispanic (NH) Black women exceeds four times that for NH whites (2–4).

Among periviable infants, small males die most frequently (5). As reported below, the mean birthweight of periviable male infants born to NH Black women has persistently fallen below that of counterparts born to NH white women.

Despite the above facts, the scientific literature includes no attempts to explain, rather than describe, the disparity in birthweight between male periviable infants born to NH Black and NH white women. Here, we offer the argument that the vanishing twin syndrome, a phenomenon in which one fetus of a twin pair dies in utero, yields small male singletons who contribute disproportionately to the disparity. We also describe evidence, found in vital statistics, consistent with our argument.

Half or more of human gestations end spontaneously without a live birth (6). The mechanisms responsible for these losses do not select randomly among fetuses. As many as 60% of those “lost” have chromosomal and genetic abnormalities (7), while slow-growing males predominate among the remainder (8–14). Natural selection presumably conserved the bias against slow-growing males because, in all societies and virtually every year for which we have dependable vital statistics, males have died in infancy more frequently than have females (15) and small male infants remain the most likely to die (5).

Historical data tracing the reproductive fitness of pregnancies show that gestations of the smallest of male infants—twins—produce the fewest grandchildren for mothers (16). The reproductive fitness of these gestations appears lowest in historic populations encountering environmental threats (e.g., poor harvests) to maternal and infant health (16). These facts have led to the argument that natural selection conserved mutations that spontaneously abort slow-growing male twins when environments become stressful (17). Contemporary empirical research supports the argument for this “selection in utero” against male twins in populations encountering an array of stressors (18–25).

Selection in utero against small male twins, a mechanism presumably conserved because it increases the reproductive fitness of women in stressful environments, need not lead to the spontaneous abortion of both fetuses. As many as 35% of twin gestations reportedly convert to “singleton” pregnancies (i.e., pregnancies gestating one fetus) via the “vanishing twin syndrome” in which the smaller fetus dies in utero (26, 27). Males predominate among vanishing twins (28). Given that most twins are same sex, males also predominate among “survivors of vanishing twin syndrome” by which we mean live born singletons who shared a fraction of their gestation with a second fetus that died in utero (29). Most important for our argument, pregnancies that convert from twin to singleton gestations via the vanishing twin syndrome produce preterm and small for gestational age (SGA) infants at a higher rate than do “true” singleton pregnancies (26, 30–36).

We know that NH Black women of reproductive age in the United States encounter more threats to maternal resources and infant health than do NH white women (37). A higher fraction of NH Black than NH white gestations of male twins should therefore convert to singleton pregnancies via the vanishing twin. Consistent with this inference, the male-to-female ratio of twins born to NH Black women before completing 27 weeks of gestation (i.e., extremely preterm) in the United States from 1995 through 2018 (i.e., 1.07) appears lower than that among twins born to NH white women (i.e., 1.16) (38).

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Selection in utero, in effect, “adds” male fetuses remaining from the vanishing twin syndrome to the population of true singletons in gestation. However, selection in utero also works against true singletons and thereby “subtracts” slow-growing, true male singletons from fetuses in gestation. The sum of these additions and subtractions could be small, thereby leaving the number of singleton male fetuses in a conception cohort essentially unchanged. As noted above, however, SGA appears more frequently among survivors of the vanishing twin syndrome than among true singletons of the same gestational age (26, 30–36). Cohorts, conceived by NH Black women, that include unexpectedly low fractions of singleton survivors of the vanishing twin syndrome should therefore yield periviable singleton males who weigh more, on average, than counterparts from other cohorts.

Attempts to empirically test the above argument require that researchers identify cohorts, conceived by NH Black women, that include unexpectedly few singleton male survivors of the vanishing twin syndrome. At least three circumstances make this a difficult task. First, much selection in utero against slow-growing and otherwise frail male twins occurs before clinical recognition of naturally conceived pregnancies. Second, while clinical records may note the vanishing of a known twin, vital statistics systems typically do not register fetal losses before the 20th week of gestation. Third, post-20th week registration of “still births” does not dependably identify a fetal death as a one of a twin set. Providing evidence for our argument therefore requires us to search vital statistics for indicators that logically, although indirectly, gauge the frequency of the vanishing twin syndrome in conception cohorts.

We believe that three plausible assumptions allow us to identify cohorts, conceived by NH Black women, from which unexpectedly few male twins vanished in utero. We assume first a sigmoid dose-response of vanishing male twins to population stressors. In the context of our argument, the *Y* axis of the dose-response diagram would show the rate of vanishing among monthly cohorts of twins conceived by NH Black women, and the *X* axis would show the dose of stress on those women. Gestations in which one fetus has a chromosomal or genetic defect will suffer vanishing regardless of the dose of stress. The response of cohorts at low stress will therefore be a plateau hovering around the “average” rate of chromosomal and genetic defects in conception cohorts. The response will then trend upward among gestations made susceptible by increasingly discordant growth rates between fetuses; the slower growing of which is male (11, 13). At some dose, however, susceptible gestations will have been depleted and the response will then hover around a plateau set by the average rate of susceptible gestations in the cohorts.

Second, we assume that the modal response among cohorts conceived by NH Black women appears closer the upper flat of the sigmoid response curve than the modal response of cohorts conceived by NH white women. We assume this because NH Black women in the United States suffer higher doses of stress than do NH white women (37).

Third, we assume that, based on the epidemiologic literature (13), most male twin fetuses “spared” from vanishing by relatively benign times will be born before 27 complete weeks of gestation (i.e., extremely preterm). Twins born after 27 complete weeks of gestation are larger, implying that they had been at low risk of vanishing and that their sex ratio at birth reflects more their ratio at conception rather than the biases of selection in utero.

These assumptions imply that decreases in population stressors on NH Black women will spare more slow-growing male twins than similar increases will “cull.” This, in turn, implies that less-stressed cohorts conceived by NH Black mothers will yield unexpectedly high sex ratios (i.e., M/F) among extremely preterm twins.

On the basis of the above, we theorize that NH Black conception cohorts that yield unexpectedly high sex ratios among extremely preterm twins will also yield male periviable singletons who include relatively few survivors of the vanishing twin syndrome. We therefore hypothesize (1) that periviable singleton males born from spared cohorts will appear heavier at birth than those born from other cohorts. We further hypothesize (2) that the disparity in birthweight between periviable singleton males born to NH Black and NH white women in these spared cohorts will appear smaller than the disparity in other cohorts. We test these hypotheses with 288 monthly conception cohorts conceived in the United States from January 1995 through December 2018.

Figure 1 summarizes the disposition, assumed by our hypotheses, of true singleton and twin conceptions in a hypothetical cohort that completed 27 weeks of gestation (i.e., through the extremely preterm period). Our independent variable is, as described in more detail below, the ratio of males to females in flow A or twin pairs that survive extremely preterm birth. Our dependent variable is the average birthweight of males in combined flows B and C or all true singletons plus survivors of the vanishing twin syndrome who survive periviable birth. We note here that the volume of flow C, controlled by the vanishing twin syndrome, can affect the characteristics of periviable male singletons born from a conception cohort (i.e., the sum of flows B and C). No mechanism, however, allows the characteristics of true singleton periviable male infants (i.e., males in flow B) to affect those of extremely preterm male twins born from a cohort (i.e., males in flow A). Our independent variable is therefore not conditioned by our dependent variable.

METHODS

Data

We retrieved restricted-use natality files that include data on all live births in the United States from the National Center of Health Statistics (NCHS), Division of Vital Statistics (38). The NCHS natality files include data on each live births’ race/ethnicity, sex, plurality (e.g., singleton and twin), gestational age, and date of birth. The University of California, Irvine Committee for the Protection of Human Subjects approved this data collection and the analyses described below (protocol no. 20195444).

Our study population included singleton and twin births to NH Black and NH white women from January 1995 through December 2019 ($N = 70,357,471$). We assigned race/ethnicity based on maternal-reported race and Hispanic ethnicity (missingness = 0.89%). We restricted our sample to extremely preterm and periviable births ($N = 506,079$; missing gestational age = 0.33%) with nonmissing birthweights ($N = 505,836$). We estimated conception month by subtracting the reported gestational weeks from the birth date (using a randomly assigned day of birth within the reported month and year of birth).

Variables

Our tests required that we identify NH Black conception cohorts that yielded unexpectedly high male-to-female sex ratios among

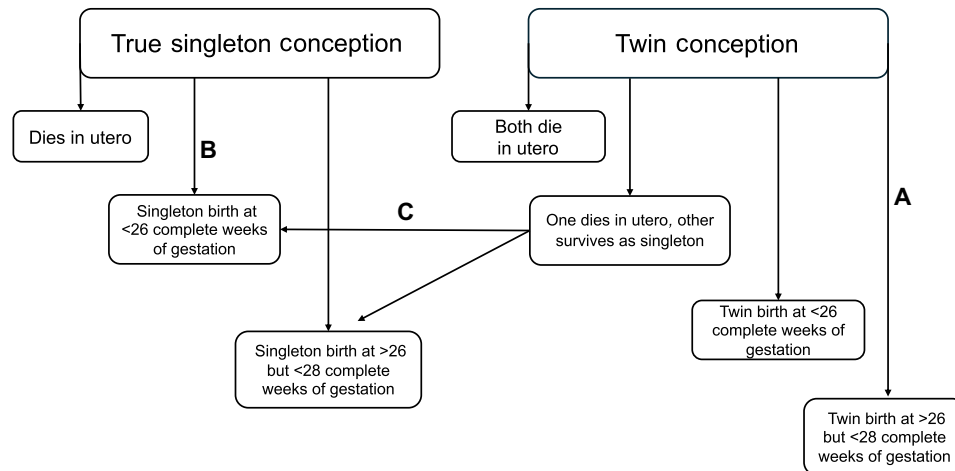


Fig. 1. Disposition of true singleton and twin conceptions in a hypothetical cohort completing 27 weeks of gestation (i.e., through the extremely preterm period of gestation).

extremely preterm twins. Twin sex ratios likely vary over time due not only to the vanishing twin syndrome but also to variation in the sex ratio at conception. We therefore defined “unexpected” sex ratios as those likely to occur by chance fewer than five times in a thousand experiments (i.e., $P < 0.005$). We assume that the sex ratio of extremely preterm twins would unlikely rise to this level unless unexpectedly many of its male members survived selection in utero. For the purposes of our test, we refer to these high outlying cohorts as spared.

We specified the outcome variable for our first hypothesis as the mean birthweight, in grams, of singleton periviable males yielded by each of 288 monthly (i.e., January 1995 through December 2018) conception cohorts conceived by NH Black women. We constructed the outcome variable for our second test by subtracting the outcome variable for our first test from the mean birthweight of singleton periviable males yielded by conception cohorts conceived by NH white women.

Statistical analyses

First, we identified conception cohorts yielding unexpectedly high sex ratios [i.e., above the $P < 0.005$ confidence interval (CI)] among extremely preterm twins born to NH Black women. Most methods for identifying such outliers assume that the values of a variable are independent from each other, thereby making their mean the expected value. Time series, however, often violate this assumption because they frequently exhibit “autocorrelation” in the form of trends, cycles (e.g., seasonality), and the tendency of high or low values to persist, although diminished, in subsequent observations. The expected value of a series exhibiting such patterns is not its mean but rather the value predicted from autocorrelation (i.e., from history). We used Box-Jenkins methods (i.e., software from Scientific Computing Associates, River Forest, IL) to detect autocorrelation in our variables and to estimate expected values (39). These methods have been widely used in the sciences including epidemiology (40–43). As described in detail elsewhere (39), Box-Jenkins models express secular trends and strong cycles (e.g., seasonality) as a function of integration, while the tendency for high or low

values to persist for relatively few time periods is expressed as moving averages, and persistence for relatively many periods is expressed as autoregression. Few time series exhibit all three types of autocorrelation. Well-defined rules determine which combination, and timing, of integration, moving averages, and autoregression best fits a series. The residuals of Box-Jenkins models, which exhibit no autocorrelation and have a mean of zero, gauge the degree to which observed values of a series differ from expected.

Second, we used the methods of Chang, Tiao, and Chen (44) to identify $P < 0.005$ outliers among the residuals of our Box-Jenkins model for sex ratios among NH Black twins born extremely preterm. These methods adjust coefficients, and residual CIs, of Box-Jenkins models to reflect the influence of outlying values on autocorrelation. We created a “spared cohort” variable scored 1 for cohorts with residuals above the $P < 0.005$ adjusted CI and 0 otherwise.

Third, we used Box-Jenkins methods to identify and model autocorrelation in the mean birthweight of the NH Black periviable singletons yielded by the 288 conception cohorts.

Fourth, we tested hypothesis 1 by estimating a Box-Jenkins “transfer function” formed by adding the spared cohort variable constructed in step 2 to the model devised in step 3. If the estimated coefficient for spared cohorts, as well as the bounds of its 95% CI, appeared positively signed, we inferred support for the hypothesis that NH Black periviable singleton males born from spared cohorts will appear heavier at birth than those born from other cohorts.

Fifth, we used Box-Jenkins methods to identify and model autocorrelation in the difference between the mean birthweight of singleton periviable males yielded by 288 conception cohorts conceived by NH white and NH Black women.

Sixth, we tested hypothesis 2 by estimating a Box-Jenkins transfer function formed by adding the spared cohort variable to the model estimated in step 5. If the estimated coefficient for spared cohorts, as well as the bounds of its 95% CI, appeared negatively signed, we inferred support for the hypothesis that NH Black conception cohorts yielding unexpectedly high sex ratios among twins born extremely preterm also yield unexpectedly small disparities in

the mean birthweight between periviable male singletons born to NH Black and NH white women.

Seventh, as a negative control outcome test, we repeated our first four steps for females rather than males. Our argument predicts a null finding because pregnancies that yield female twins appear more reproductively fit than those that produce singletons (16, 17). Selection in utero would therefore unlikely select as strongly against female twins as against male twins.

RESULTS

The first two steps in our analyses identified cohorts, conceived by NH Black women, likely to include relatively few live born male singletons who shared a fraction of their gestation with a second fetus that died in utero. As noted above, we defined these spared cohorts as those with very high sex ratios of extremely preterm twins. That ratio for the entire population of extremely preterm twins born to NH Black women during our test period was 1.06 compared to 1.17 for counterparts born to NH white women. The ratio for the 288 conception cohorts born to NH Black women ranged from 0.61 to 1.96 with a mean, as expected from the population, of 1.06. Figure 2 shows, as points, the sex ratio plotted over the test period.

The results of step 1 in our analyses, in which we identified autocorrelation in the sex ratio of twins born extremely preterm to NH Black women, appear in Table 1. As shown, the ratio exhibited autocorrelation in the form of autoregression in which a high or low value at month t predicted a high or low value, although diminished, 5 months later (i.e., at $t+5$). Figure 2 shows, as a line, the expected values estimated by the Box-Jenkins model.

Step 2, in which we searched for $P < 0.005$ outliers in the residuals from the Box-Jenkins model estimated in step 1, found nine values (shown in Fig. 2 as triangles) outside the CI. We note that two (i.e., 1 high and 1 low) outliers would be expected by chance

(i.e., $288 \times 0.005 = 1.44$). As shown in Fig. 1 and consistent with the assumptions noted above (i.e., high stress load among NH Blacks and sigmoid dose-response of vanishing twins to maternal stress), we found two low but seven high outliers. We used these high outliers to create a spared cohort variable scored 1 for the high outlying cohorts and 0 otherwise.

In steps 3 and 4, we tested the hypothesis that, among cohorts conceived by NH Black women, the seven identified in step 2 as spared will yield heavier periviable male singletons than will other cohorts. Table 2 shows the mean birthweight for those infants, as well as for several other groups, over the 288 conception cohorts. Table 1 shows the parameters of the best-fitting Box-Jenkins model, estimated in step 3, for the mean birthweight of periviable male singletons yielded by the conception cohorts conceived by NH Black women. As shown, the series exhibited complex autocorrelation including not only a moving average at $t-9$ but also seasonality (i.e., autoregression at $t-12$) and the tendency for high or low values to persist into the subsequent month (i.e., autoregression at $t-1$). Table 3 shows the results of step 4 in which we test our first hypothesis. As shown, we found support for the hypothesis in that the estimated coefficient for spared cohorts (i.e., 34.1 g), as well as the bounds of its 95% CI (i.e., 8.9; 59.3), were all positively signed. The mean birthweight of the seven spared cohorts was 762 g, implying an average cohort gain of ~4.5%.

In steps 5 and 6, we tested the hypothesis that the seven cohorts identified in step 2 as spared will yield relatively small disparities in birthweight between periviable singleton males conceived by NH Black and NH white women. That disparity (i.e., periviable males conceived by NH white women minus those conceived by NH Black women) ranged over the cohorts from -124 to 172 g with a mean of 30 g. Figure 3 shows, as points, the disparity plotted over the 288 monthly conception cohorts. Table 1 shows the results of step 5, in which we used Box-Jenkins methods to identify and model

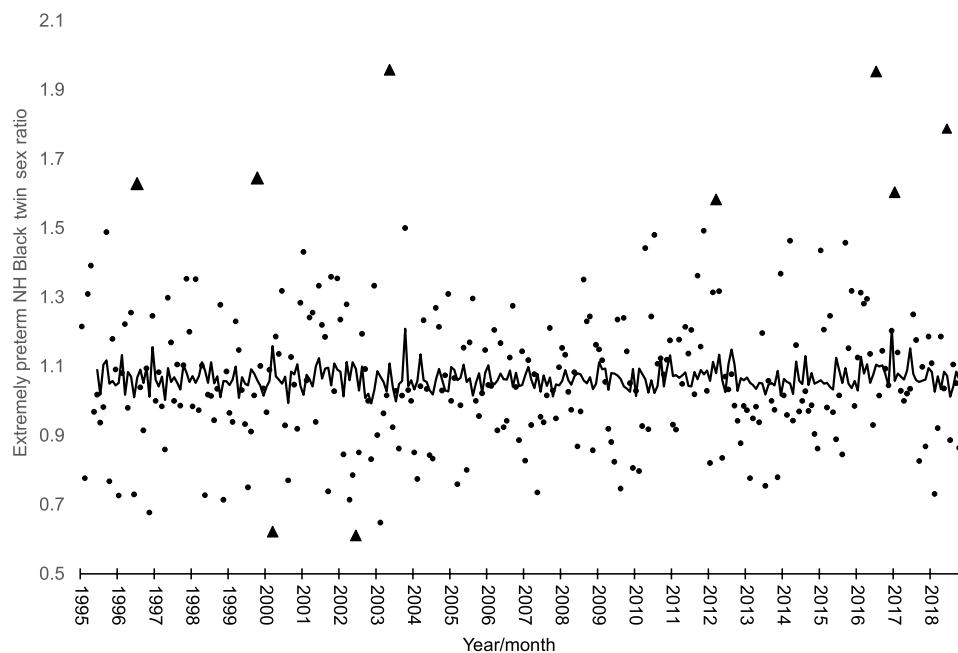


Fig. 2. Expected (line) and observed (points) sex ratio of extremely preterm NH Black twins yielded by 288 monthly US conception cohorts (January 1995 through December 2018). Outlying ($P < 0.005$) cohorts shown with triangles. First five cohorts lost to modeling.

Table 1. Estimated coefficients (95% CI in parentheses) for time-series models of test variables describing 288 conception cohorts begun in the United States from January 1995 to December 2018.

Variable	Sex ratio extremely preterm twins born to NH Black women	Mean birthweight periviable singleton males born to NH Black women	Birthweight of periviable male singletons born to NH white women less birthweight of periviable male singletons born to NH Black women
Constant	1.046 (1.022;1.070)	726.8 (719.5; 734.1)	35.1 (24.7; 45.5)
Moving average	None	$t-9 = -0.186 (-0.304; -0.068)$	None
Autoregression	$t-5 = 0.168 (0.058; 0.277)$	$t-1 = 0.125 (0.007; 0.243)$ $t-12 = 0.220 (0.106; 0.334)$	$t-4 = 0.165 (0.043; 0.287)$ $t-9 = 0.225 (0.105; 0.345)$ $t-12 = 0.139 (0.012; 0.256)$

Table 2. Means of cohort mean birthweight (in grams) of infants (grouped by maternal race, plurality of birth, and sex) yielded by 288 monthly conception cohorts begun in the United States from January 1995 to December 2018.

Maternal race	Plurality of birth	Sex	Means of cohort mean birthweight (g)
NH Black	Periviable singletons	Male	729
		Female	716
	Extremely preterm twins	Male	655
		Female	634
NH white	Periviable singletons	Male	760
		Female	741
	Extremely preterm twins	Male	687
		Female	662

Table 3. Estimated coefficients (95% CI in parentheses) for time-series models describing 288 conception cohorts begun in the United States from January 1995 to December 2018.

	Dependent variable	
	Mean birthweight periviable singleton males born to NH Black women	Mean birthweight periviable singleton males born to NH white women less that of those born to NH Black women
Constant	725.2 (718.1; 732.2)	37.6 (27; 48.2)
Spared cohorts	34.1 (8.9; 59.3)	-57.4 (-93.4; -21.4)
Moving average	$t-9 = -0.184 (-0.304; -0.064)$	None
Autoregression	$t-1 = 0.125 (0.007; 0.243)$ $t-12 = 0.209 (0.093; 0.325)$	$t-4 = 0.198 (0.076; 0.320)$ $t-9 = 0.223 (0.101; 0.345)$ $t-12 = 0.134 (0.011; 0.257)$

autocorrelation in the disparity series. This series exhibited complex autocorrelation including not only autoregression at $t-9$ and seasonality (i.e., autoregression at $t-12$) but also an “echo” such that high or low values tended to repeat, although diminished, 4 months later (i.e., autoregression at $t-4$). Figure 3 shows, as a line, the expected values yielded by the Box-Jenkins model.

Table 3 shows the results of step 6, in which we test the hypothesis that the seven cohorts identified in step 2 as spared will yield relatively small disparities in birthweight between periviable males

conceived by NH Black and NH white women. As shown, we found support for the hypothesis in that the estimated coefficient for spared cohorts (i.e., -57.4 g), as well as the bounds of its 95% CI (i.e., -93.4; -21.4), all appeared negatively signed. To add context to this finding, we note that the estimated average decrease below the expected disparity among the seven spared cohorts (i.e., 57 g) exceeds the average NH white advantage among the other 276 cohorts (i.e., 32 g).

In step 7, a negative outcome control test, we repeated our test of hypothesis 1 for females rather than males. Our argument predicts a

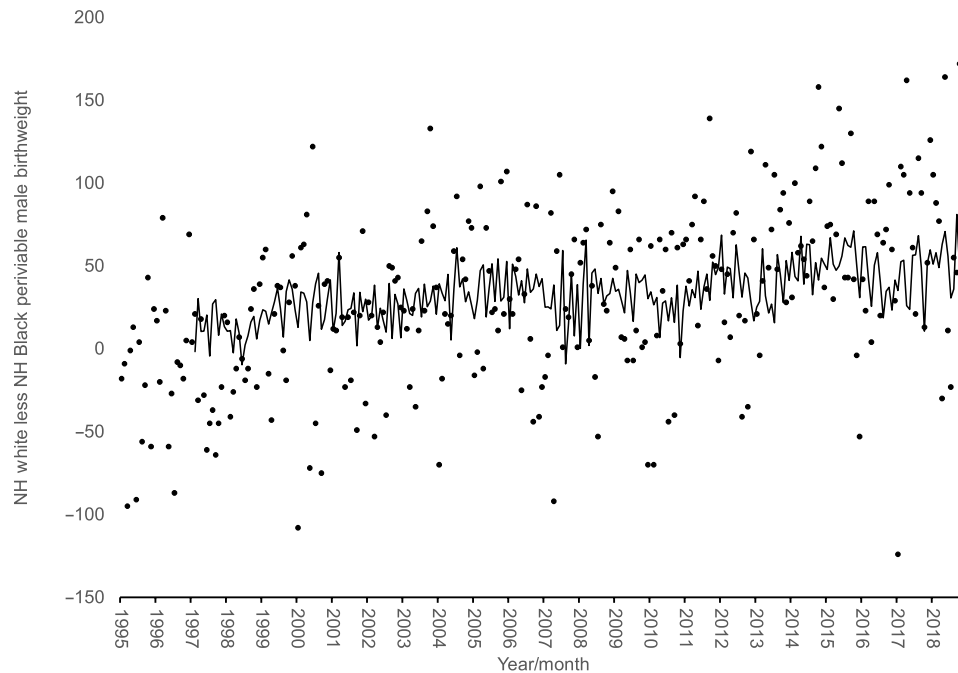


Fig. 3. Expected (line) and observed (points) difference (i.e., NH white–NH Black) in periviable male mean birthweight (in grams) for 288 monthly conception cohorts (January 1995 through December 2018). First 25 cohorts lost to modeling.

null finding because pregnancies that yield female twins appear more reproductively fit than those that produce singletons (16). Selection in utero would therefore unlikely select as strongly against female twins as against male twins. Consistent with our expectation, we found no association between the NH Black periviable twin sex ratio and the mean birthweight of NH Black periviable female births (i.e., coefficient for spared cohorts = 1.6 g; 95% CI, –27; 30).

We also repeated our test of hypothesis 1 but added a binary predictor variable scored 1 for the two cohorts with unexpectedly low periviable twin sex ratios. We did this to determine if, as expected, the association would appear too small or insufficiently stable to be confidently detected. Consistent with expectations, the bounds of the 95% CI (i.e., –71.7; 21.9) of the coefficient (i.e., –30) were both negatively and positively signed.

DISCUSSION

In the United States, male periviable singletons born to NH Black women weigh less than counterparts born to NH white women. On the basis of evolutionary theory and epidemiologic facts, we argue that selection in utero, via the vanishing twin syndrome, likely contributes to this disparity. Consistent with our argument, we found that male periviable singletons born to NH Black women weigh more at birth and that the disparity between them and their counterparts born to NH white women appears smaller in conception cohorts that likely include relatively few survivors of the vanishing twin syndrome. This finding would seem important given that small periviable males more likely die in the first year of life than other infants.

We acknowledge weaknesses in our argument and tests. We know, for example, that the extremely preterm twin sex ratio only indirectly gauges the depth of selection against small male twins. We used this indicator because we are epidemiologists and demographers and the

literature in our fields reports that the ratio gauges selection in utero against less fit fetuses (17–25). We urge researchers from other fields to devise better indicators but warn those inclined to the task that, with the exception of gestations begun via assisted reproductive technology, losses of twins in utero cannot be counted because most occur before clinical recognition of pregnancy.

We also acknowledge that we cannot statistically control unmeasured confounders. Our findings, however, could not spuriously arise from autocorrelation shared with confounders or from any confounder that affects the birthweight of periviable females born to NH Black women or periviable males born to NH white women. We know of no potential confounder that varies randomly in time and affects the “production” of extremely preterm male, but not female, twins born to NH Black women while simultaneously modifying the birthweight of periviable male singletons born to NH Black, but not NH white, women.

We focused on NH Black males for two reasons. First, male-to-female ratios among preterm, twin, and small-for-gestational age births in the United States all appear lowest for NH Blacks (45). The fact that this male “missingness” occurs among the frailest live births lends support to the assumption of relatively deep selection in utero against small Black males. Second, Black periviable males surviving birth die more frequently in the first year of life than other infants of either sex or any race/ethnicity (2, 3). Focusing on understanding antecedents of variation in weight among the frailest (i.e., periviable) of NH Black male infants would therefore seem important for public health.

The association we found may not confirm our argument but does, particularly in light of the lethality of small size among periviable infants, justify further exploration of the contribution of the vanishing twin syndrome to disparities in birth outcomes. Although societal concern over these disparities motivated us to focus on US

NH Blacks, the logic of our “vanishing twin” argument applies to male gestations of any highly stressed population. Our test, however, requires monthly conception cohorts large enough to yield dependable estimates of autocorrelation in the sex ratio of extremely preterm twins. This circumstance would likely lead to replication efforts using relatively large populations or smaller populations with aggregation of conception cohorts into quarters or years.

We anticipate and hope that our findings will lead to the question of how the vanishing twin syndrome affects the disparity in mortality between infants born to NH Black and white women. The data needed for those estimations are currently not available to us. Much controversy remains, moreover, as to the functional form of the relationship between weight and infant mortality among periviable infants because gestational age within the periviable range, plurality (i.e., singleton v twin), infant sex, and maternal education all moderate the association (46). The association also differs between true singletons and known singleton survivors of the vanishing twin syndrome (30–36).

Our argument and findings suggest that the vanishing twin syndrome contributes to the disparity in birthweight between periviable males conceived by NH Black and NH white women. That syndrome, however, appears only one among several mechanisms plausibly conserved by natural selection to suppress reproduction among populations confronted with threats to the well-being of women and infants (47, 48). Because historical and contemporary racism manifests both in a high dose and a wide variety of threats to the well-being of NH Black Americans, isolating and mitigating specific drivers of selection in utero among them will likely prove difficult. It would seem important to therefore increase access to perinatal care, delivered without racial biases (49), for pregnant people at risk of vanishing twin syndrome (50). We note, however, that twin fetuses “rescued” from the vanishing twin syndrome and delivered extremely preterm will be relatively frail at birth. Sustaining them will require expensive neonatal intensive care (51). Even with this care, they will exhibit relatively high rates of infant mortality and childhood morbidity (5).

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