Original Article

Male-to-Female Ratios, Race/Ethnicity, and Spontaneous Preterm Birth among 11 Million California Infants

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Abstract

Objective An observed disparity in population-scale data are a larger number of males among preterm births (PTBs). We investigated spontaneous PTB risk among women of various race/ethnic groups in combination with infants' sex.

Study Design This observational study was conducted in > 10 million California births (1991–2012) using birth certificates linked with maternal and infant hospital discharge data.

Results Male-to-female ratios among term (37–42 weeks) infants exhibited the narrow ratio range 1.02 to 1.06 across race/ethnic groups. Such ratios among spontaneous PTBs were generally larger for all race/ethnic groups except non-Hispanic blacks. For blacks, ratios tended to be lower and similar to their term birth counterpart, 1.03. Hazard ratios adjusted for maternal age and education for non-Hispanic blacks were 0.99 (95% confidence interval [CI] 0.90–1.09), 1.01 (95% CI 0.95–1.08), 0.98 (95% CI 0.94–1.03), and 1.03 (95% CI 1.01–1.05), respectively, for gestational week groupings of 20 to 23, 24 to 27, 28 to 321, and 32 to 36. Hazard ratios for non-Hispanic whites for the same groupings were 1.08 (95% CI 0.98–1.18), 1.13 (95% CI 1.07–1.19), 1.21 (95% CI 1.17–1.25), and 1.18 (95% CI 1.17–1.19).

Conclusion Why male-to-female ratios are similar across gestational ages in blacks but substantially higher in other race/ethnic groups is theoretically considered relative to inflammation, stress, and other influences.

Keywords
- secondary sex ratio
- disparity
- prematurity
- pregnancy

Preterm birth (PTB, delivery before 37 weeks' gestation) is associated with substantial morbidity and mortality with a global burden of > 15 million babies born preterm every year.[1] In the U.S., PTB occurs in approximately 10% of live births.[2] Part of the population occurrence of PTB can be attributed to maternal or fetal conditions requiring medical intervention to facilitate earlier delivery. However, risk factors for *spontaneous* PTB remain largely unexplained. Potential factors identified for spontaneous PTB have included race, infection, stress, genetics, and selected environmental toxicants.[3] Each of these broad range of factors has either explained only a small fraction of the population burden or has been insufficiently studied to derive clear inferences.

Several investigations have attempted, with only limited success, to identify contributing factors for the observed elevated occurrence of spontaneous PTB among U.S. blacks

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compared with non-Hispanic whites. As an example, in a recent investigation from our group, we observed the prevalence ratio (blacks relative to non-Hispanic whites) in California to be 1.4 for moderate spontaneous PTB (32–36 weeks' gestation) and 3.0 for early spontaneous PTB (20–31 weeks).[4] However, in that work we generally did not observe evidence to suggest that variability in numerous markers of social disadvantage contributed to these prevalence disparities.[4]

Another prevalence disparity that has been observed from population-scale data are a disproportionate number of males among PTBs, particularly early spontaneous PTB, that is, < 32 weeks' gestation.[5–7] Underlying mechanisms for this sex disparity are not well understood. Possible reasons put forth for such sex differentials in spontaneous PTBs include intrauterine inflammation or infection-response associated with higher concentrations of proinflammatory markers in male infants[8–11] as well as variability in selection pressures on females or males to survive to term gestation.[12]

To our knowledge, we are not aware of studies that have specifically investigated risks of spontaneous PTB among U.S. black women in combination with the sex of their infants. Here we make such inquiries among more than 10 million births in California in the period 1991 to 2012.

Materials and Methods

Study Population

Data for this retrospective cohort study come from the Office of Statewide Health Planning and Development California birth cohort files for 1991 to 2012. These files contain merged birth/stillbirth (i.e., gestational age > 19 weeks), and infant death certificates for nearly all vital records in California linked with maternal and infant hospital discharge data at delivery. Over this time period, there was a total of 11,724,817 live birth and stillbirth deliveries. We restricted the study to those with gestational ages 20 to 42 weeks determined by last menstrual period, with plausible birth weight for gestational age,[13] and whose sex was not missing ($n = 11{,}047{,}048$). Gestational age was missing or outlier for approximately 8% of all singleton deliveries. For our main analyses of spontaneous PTB, records were required to be linked with the maternal hospitalization record ($n = 10{,}658{,}214$). Analyses containing stillbirth data were limited to 1991 to 2011 and did not exclude records with implausible birth weight ($n = 10{,}291{,}926$). For sensitivity analysis that considered prepregnancy maternal body mass index (BMI) and maternal cigarette smoking, data were limited to years 2007 to 2012 and gestational age was based on the obstetric estimate (best obstetric estimate was unavailable before 2007 births).

Data for maternal race/ethnicity were extracted from the birth certificate and categorized as non-Hispanic white, non-Hispanic black, Asian, Pacific Islander, Hispanic, American Indian/Alaskan Native, other, and missing. Data for paternal race/ethnicity were also considered (non-Hispanic white, non-Hispanic black, Asian, Pacific Islander, Hispanic, American Indian/Alaskan Native, other, and missing). Having both parents' race/ethnic background offered a means to explore potential maternal or paternal differences in sex ratios. Prepregnancy BMI was calculated as (weight in pounds / height^2 in inches) $\times$ 703 based on self-reported weight and height on the birth certificate. Standard BMI ranges were applied such that normal was defined as 18.5 to 25 kg/m^2 and obese defined as $\geq$ 30 kg/m^2. Maternal education was categorized as some high school or less, high school graduate or equivalent, some college, and college graduate or more. Maternal age was in years and entered as a continuous variable in adjusted analyses.

Our analytic goal was to specifically investigate *spontaneous* PTB. Thus, the case group was further restricted to spontaneous PTB events based on information coded on hospital discharge or birth certificate records. Spontaneous PTB was identified as those births < 37 weeks with preterm premature rupture of membranes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 658.1 or birth certificate complication of labor/delivery code 10), premature labor (ICD-9-CM code 644), or the use of tocolytics (birth certificate complication/procedure of pregnancy code 28). PTBs were more narrowly defined as 20 to 23 gestational weeks, 24 to 27 weeks, 28 to 31 weeks, or 32 to 36 weeks.

Analysis

Cox proportional hazards regression was modeled with gestational age in completed weeks as the underlying time and estimated the hazard ratio (HR) and 95% confidence interval (95%CI) of PTB for male infant sex versus female (referent). Given the shortest gestation recognized by California was 20 weeks for a live birth and stillbirth alike, time zero was set as 19 weeks. Deliveries reaching 37 weeks' gestational age were censored. Individual models for each maternal race/ethnicity were performed. Similarly, models adjusted for maternal age (mothers < 13 or > 55 years old were excluded) and education (excluded if education was missing) were performed.

Analysis of PTB at 20 to 23, 24 to 27, 28 to 31, and 32 to 36 gestational weeks was conditional on not being delivered prior to the gestational age lower bound. Additionally, deliveries after the gestational age upper bound were censored at that time. For example, analysis of PTB 28 to 31 weeks included deliveries $\geq$ 28 weeks with deliveries reaching 32 weeks being censored.

Analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, N.C., 2015–2016).

Missing Data

The covariates considered in primary analyses were maternal race/ethnicity, age, and education. None of these variables had > 5% missing values. The covariate of BMI equal to obesity did have a frequency of missing values for more than 5% of study subjects. However, given that our use of this variable was for sensitivity analysis, we did not attempt to use imputation methods to address the absence of data due to missing values.

Ethics Approval

This study was approved by the Stanford University Institutional Review Board and the California State Committee for the Protection of Human Subjects.

Table 1 Male-to-female ratios among live born offspring of California mothers by race/ethnicity and gestational age at delivery (spontaneous preterm birth), 1991–2012

Maternal race/ethnicity	Infant sex	20–23 wk		24–27 wk		28–31 wk		32–36 wk		37–42 wk		% < 37 wk
		N	M:F	*N*	M:F	*N*	M:F	*N*	M:F	*N*	M:F	
Non-Hispanic white	M	1,057		3,207		7,552		60,943		1,528,638		4.38
	F	934	1.13	2,675	1.20	5,914	1.28	49,058	1.24	1,459,544	1.05	3.73
Non-Hispanic black	M	901		2,078		3,486		15,842		276,005		6.95
	F	875	1.03	1,987	1.05	3,424	1.02	14,878	1.06	267,631	1.03	6.84
Asian	M	400		1,261		3,134		24,938		549,188		4.91
	F	363	1.10	947	1.33	2,281	1.37	19,077	1.31	518,692	1.06	4.02
Pacific Islander	M	34		69		199		1,081		23,992		5.11
	F	20	1.70	89	0.78	146	1.36	842	1.28	22,825	1.05	4.32
Hispanic	M	2,502		6,705		14,709		93,477		2,327,504		4.53
	F	2,207	1.13	5,638	1.19	11,210	1.31	73,671	1.27	2,263,381	1.03	3.73
American Indian/ Alaskan Native	M	20		59		164		995		19,823		5.51
	F	22	0.91	49	1.20	110	1.49	808	1.23	19,366	1.02	4.60
Other	M	3		9		16		148		3,131		5.03
	F	6	0.50	12	0.75	15	1.07	122	1.21	3,037	1.03	4.60

Results

As shown in ►Table 1, the male-to-female ratio among term (37–42 weeks) infants is slightly above 1.0 and exhibits a very narrow range from 1.02 to 1.06 across the various maternal race/ethnic groups in California. However, the male-to-female ratio among spontaneous PTBs (gestational ages < 37 weeks) was observed to be further above 1.0. Among the PTB groups, a male-to-female ratio larger than 1.0 is observed for all race/ethnic groups, except non-Hispanic blacks. For non-Hispanic blacks, the male-to-female ratio is fairly constant across all PTB gestational age groups and quite similar to its 1.03 counterpart among term births. These male-to-female ratios for spontaneous PTBs are reflected by HRs in ►Table 2 with the observed relations remaining after adjustment for maternal age and education.

The male-to-female ratio pattern observed for spontaneous PTBs was also observed for overall PTB, that is, both spontaneous and medically indicated (►Supplementary Tables S1 and S2, available in the online version).

The lower male-to-female ratio observed for spontaneous PTB categories, particularly among non-Hispanic blacks, appeared to be driven slightly more by race/ethnicity of the mother than by the father as shown in ►Table 3. However, some of these comparisons were subject to a sizable amount of variability owing to small cell sizes (see ►Table 4 for HRs).

We explored whether the observed male-to-female ratio pattern in ►Tables 1 and 2 was influenced by maternal smoking or by prepregnant obesity (i.e., BMI > 30). Further adjustment for smoking did not materially change the observed results (not shown). With regard to obesity, although results among obese women (BMI > 30) were much more variable in the very earliest gestational age category (20–23 weeks) likely owing to small numbers, for the most part the other gestational age categories mimicked the pattern observed overall (►Supplementary Table S3, available in the online version).

Table 2 Hazard ratios for male infant sex among live born offspring of California mothers by race/ethnicity and gestational age at delivery (spontaneous preterm birth), 1991–2012

Maternal race/ethnicity	20–23 wk		24–27 wk		28–31 wk		32–36 wk	
	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI
Non-Hispanic white	1.08	0.98, 1.18	1.13	1.07, 1.19	1.21	1.17, 1.25	1.18	1.17, 1.19
Non-Hispanic black	0.99	0.90, 1.09	1.01	0.95, 1.08	0.98	0.94, 1.03	1.03	1.01, 1.05
Asian	1.03	0.89, 1.19	1.22	1.12, 1.33	1.28	1.22, 1.36	1.22	1.20, 1.25
Pacific Islander	1.50	0.86, 2.63	0.68	0.49, 0.94	1.28	1.03, 1.59	1.21	1.10, 1.32
Hispanic	1.09	1.03, 1.16	1.14	1.10, 1.18	1.26	1.23, 1.29	1.22	1.21, 1.24
American Indian/Alaskan Native	0.83	0.45, 1.53	1.18	0.81, 1.73	1.45	1.14, 1.85	1.19	1.08, 1.30
Other	0.50	0.12, 1.98	0.72	0.30, 1.71	0.96	0.47, 1.97	1.16	0.91, 1.47

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]Hazard ratio adjusted for maternal age and education.

Table 3 Male-to-female ratios among live born offspring of California parents by race/ethnicities and gestational age at delivery (spontaneous preterm birth), 1991–2012

Maternal race/ethnicity[a]	Paternal race/ethnicity[b]	Infant sex	20–23 wk		24–27 wk		28–31 wk		32–36 wk		37–42 wk	
			N	M:F	*N*	M:F	*N*	M:F	*N*	M:F	*N*	M:F
Non-Hispanic white	Non-Hispanic white	M	757		2,317		5,567		47,522		1,213,664	
		F	649	1.17	1,943	1.19	4,311	1.29	37,840	1.26	1,154,857	1.05
	Non-Hispanic black	M	42		135		259		1,639		38,440	
		F	46	0.91	110	1.23	217	1.19	1,458	1.12	37,997	1.01
	Other	M	166		541		1,224		8,966		222,508	
		F	183	0.91	464	1.17	987	1.24	7,300	1.23	214,258	1.04
Non-Hispanic black	Non-Hispanic white	M	41		63		133		703		12,288	
		F	32	1.28	88	0.72	127	1.05	574	1.22	11,626	1.06
	Non-Hispanic black	M	716		1,685		2,738		12,324		217,360	
		F	688	1.04	1,574	1.07	2,687	1.02	11,567	1.07	210,322	1.03
	Other	M	42		86		181		873		16,502	
		F	41	1.02	95	0.91	154	1.18	789	1.11	16,140	1.02
Asian	Non-Hispanic white	M	48		171		461		4,005		69,748	
		F	41	1.17	133	1.29	295	1.56	3,026	1.32	66,986	1.04
	Non-Hispanic black	M	12		50		89		597		9,269	
		F	14	0.86	31	1.61	75	1.19	516	1.16	9,077	1.02
	Other	M	327		988		2,418		19,503		455,258	
		F	292	1.12	741	1.33	1,808	1.34	14,851	1.31	428,223	1.06
Pacific Islander	Non-Hispanic white	M	6		6		30		181		4,028	
		F	1	6.00	14	0.43	23	1.30	158	1.15	3,836	1.05
	Non-Hispanic black	M	3		9		23		96		2,031	
		F	1	3.00	7	1.29	19	1.21	81	1.19	1,963	1.03
	Other	M	23		44		127		717		16,528	
		F	16	1.44	66	0.67	95	1.34	532	1.35	15,680	1.05
Hispanic	Non-Hispanic white	M	148		422		1,037		7,264		163,793	
		F	129	1.15	379	1.11	717	1.45	5,602	1.30	157,504	1.04
	Non-Hispanic black	M	76		179		358		1,807		37,299	
		F	68	1.12	148	1.21	253	1.42	1,606	1.13	37,001	1.01
	Other	M	2,100		5,661		12,184		78,182		1,994,627	
		F	1,883	1.12	4,714	1.20	9,420	1.29	61,208	1.28	1,938,933	1.03
American Indian/ Alaskan Native	Non-Hispanic white	M	3		10		43		337		6,453	
		F	7	0.43	14	0.71	34	1.26	243	1.39	6,383	1.01
	Non-Hispanic black	M	1		6		24		66		1,271	
		F	2	0.50	6	1.00	11	2.18	67	0.99	1,254	1.01
	Other	M	13		37		77		484		10,225	
		F	10	1.30	20	1.85	51	1.51	403	1.20	9,829	1.04

[a]Maternal race/ethnicity "other" and "missing" not shown owing to small numbers.
[b]Paternal race/ethnicity "missing" not shown owing to small numbers.

These BMI analyses were restricted to births in the period 2007 to 2012 because BMI information was not collected on the entire study cohort.

We also explored whether our limiting analyses to live born only births influenced results. Thus, we repeated analyses shown in ►Table 1 by including both stillbirths and live births. Those results are shown in ►Supplementary Tables S4 and S5 (available in the online version). These analyses showed similar male-to-female ratios patterns as observed for live births only, that is, similar male-to-female ratios across all gestational ages for blacks, but not other race/ethnic groups.

Conclusion

We examined associations between women's race/ethnicity and the male-to-female ratio among their offspring spontaneously delivered at various gestational ages in approximately 10 million California births. We observed a male-to-female

Table 4 Hazard ratios for male infant sex among live born offspring of California parents by race/ethnicities and gestational age at delivery (spontaneous preterm birth), 1991–2012

Maternal race/ethnicity[a]	Paternal race/ethnicity[b]	20–23 wk		24–27 wk		28–31 wk		32–36 wk	
		HR[c]	95% CI	HR[c]	95% CI	HR[c]	95% CI	HR[c]	95% CI
Non-Hispanic white	Non-Hispanic white	1.10	0.99, 1.22	1.12	1.06, 1.19	1.22	1.17, 1.27	1.19	1.17, 1.20
	Non-Hispanic black	0.89	0.59, 1.36	1.20	0.93, 1.55	1.17	0.98, 1.40	1.10	1.03, 1.19
	Other	0.86	0.70, 1.07	1.11	0.98, 1.26	1.18	1.09, 1.29	1.18	1.14, 1.21
Non-Hispanic black	Non-Hispanic white	1.20	0.76, 1.90	0.67	0.49, 0.93	0.98	0.77, 1.25	1.15	1.03, 1.28
	Non-Hispanic black	1.00	0.90, 1.11	1.03	0.96, 1.11	0.98	0.93, 1.04	1.03	1.00, 1.05
	Other	0.99	0.64, 1.52	0.89	0.66, 1.19	1.14	0.92, 1.41	1.07	0.98, 1.18
Asian	Non-Hispanic white	1.10	0.73, 1.67	1.21	0.97, 1.52	1.47	1.27, 1.71	1.26	1.20, 1.32
	Non-Hispanic black	0.83	0.38, 1.79	1.56	1.00, 2.44	1.15	0.84, 1.56	1.13	1.00, 1.27
	Other	1.04	0.89, 1.22	1.24	1.12, 1.36	1.24	1.17, 1.32	1.22	1.20, 1.25
Pacific Islander	Non-Hispanic white	5.65	0.68, > 9.9	0.41	0.16, 1.07	1.23	0.72, 2.12	1.09	0.88, 1.34
	Non-Hispanic black	2.91	0.30, > 9.9	1.23	0.46, 3.30	1.15	0.63, 2.12	1.14	0.85, 1.54
	Other	1.34	0.71, 2.54	0.62	0.42, 0.91	1.25	0.96, 1.63	1.26	1.13, 1.41
Hispanic	Non-Hispanic white	1.09	0.86, 1.38	1.06	0.92, 1.21	1.37	1.25, 1.51	1.24	1.20, 1.28
	Non-Hispanic black	1.09	0.79, 1.51	1.18	0.95, 1.47	1.38	1.18, 1.63	1.11	1.04, 1.18
	Other	1.07	1.00, 1.14	1.15	1.11, 1.20	1.24	1.21, 1.27	1.23	1.22, 1.24
American Indian/ Alaskan Native	Non-Hispanic white	0.41	0.11, 1.59	0.68	0.30, 1.54	1.22	0.78, 1.91	1.34	1.14, 1.58
	Non-Hispanic black	0.49	0.04, 5.39	0.97	0.31, 3.02	2.13	1.04, 4.35	0.97	0.69, 1.36
	Other	1.23	0.54, 2.81	1.74	1.01, 3.01	1.43	1.01, 2.04	1.15	1.00, 1.31

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]Maternal race/ethnicity "other" and "missing" not shown owing to small numbers.
[b]Paternal race/ethnicity "missing" not shown owing to small numbers.
[c]Adjusted for maternal age.

ratio substantially larger than 1.0 for spontaneous PTB in all race/ethnic groups except non-Hispanic blacks. For non-Hispanic blacks, the male-to-female ratio was fairly constant across all gestational age groups and quite similar to its 1.03 counterpart among term births.

Cooperstock and Campbell[5] appear to have been the first to describe associations between women's race/ethnicity, male-to-female ratios, and overall PTB. Their study population included > 2 million black and white births (1977–1988) in 6 New England U.S. states. These investigators observed an excess of males among PTBs—with the excess considerably larger for white than for black infants. The noted excess of males among PTBs was influenced by maternal age, maternal education, and marital status among whites but not among blacks. Chien et al in 2011[14] investigated nearly 4 million U.S. singleton 2002 births and observed male-to-female ratios to be higher among all PTBs (20–36 weeks combined) for all race/ethnic groups, but less pronounced among black infants and more pronounced among Hispanic infants. PTBs in each of these studies included all PTB phenotypes, that is, indicated or spontaneous, whereas our focus in the current study was primarily on spontaneous PTB.

The explanation of our overall observed results is not obvious, that is, why does the male-to-female (secondary sex) ratio appear to be similar across gestational ages in blacks but is substantially higher in other race/ethnic groups for earlier gestational ages? As Eriksson et al[15] note, males tend to grow faster in utero and therefore may place them at greater risk than females under less favorable conditions such as undernourishment. Other less favorable in utero conditions like inflammation and stress might capitalize on such vulnerability. Thus, one possible explanation may be a result of women's inflammatory milieu during pregnancy. Recently, Radin et al[16] observed in a randomized trial that women's inflammation (as measured by serum concentration of C-reactive protein) was associated with lowered survival of male fetuses (i.e., reduced male-to-female ratio) and that low-dose aspirin may modulate such an association via reducing inflammation. If black women were in general to experience more inflammation during pregnancy, this would explain both a lowered male-to-female ratio in early preterm infants as well as a higher frequency of PTB overall among this population group.

Evans and Myatt[17] offer an oxidative stress mechanism for altered male-to-female ratios, particularly where males appear to be associated with adverse pregnancy outcomes. They observed a modifying influence by maternal obesity via oxidative stress in that among nonobese women, a male fetus had the highest antioxidant activity whereas among the obese, a male fetus did not have the same level of potential protective antioxidant activity. Although we did not observe the male-to-female ratio by race/ethnicity patterns to be different based on maternal strata of maternal prepregnancy

BMI, that is, obese, further investigations of how this novel mechanism might contribute to male-to-female differences between blacks and whites seems warranted.

Another "mechanistic" interpretation that could be put forward is that black women may undergo more ambient stressors in their daily lives. Prenatal ambient stressors such as earthquakes, terrorist attacks, bomb alarms, and economic fluctuations have been associated with an increase in females, that is, a lowered male-to-female secondary sex ratio, among infants delivered preterm.[18–21] James[22] has proposed that stress experienced by pregnant women results in selective loss of male fetuses and that mechanistically stress is mediated through higher androgen levels. Ingemarsson[23] notes that fetal males contribute to the onset of preterm labor with suggested mechanisms involving androgen precursors and antagonists to interleukin-1 receptors. How such mechanisms might differ between blacks and whites cannot be determined from the current data. Nevertheless, these mechanistic paradigms may be important to explore in black women in the U.S. as an underlying contributor to the lowered male-to-female ratio in blacks compared with whites among preterm infants. Further, these lines of inquiry may have alignment with the "weathering hypothesis" that indicates black women, based on certain at-risk behaviors as well as deprived social circumstances, may develop accelerated biologic aging that could affect the risk of PTB overall.[24] Goodman et al, for example, have argued that the depleted stress response commonly attributed to weathering implies attenuated selection in utero against small for gestational age male fetuses.[25] They report evidence of attenuated selection among African American males born in California.[25] If real, this attenuation could, in part, explain our findings because early PTBs among African American women would include relatively few spontaneous abortions induced by selection in utero.

Goodman et al's "weathering" argument implies a more general explanation, based on selection in utero.[12] Differences among race/ethnicity groups in the timing of such selection could explain the sex ratios we observe if loss or stillbirth of male fetuses destined to be born preterm occurs earlier among black than other women. Others have described the construct of live birth selection bias.[26] Although this selection proposition seems plausible, it is mostly unmeasurable in that data on all conceptions at a population scale are not available. Of note, in the current study we did explore the impact of stillbirths on findings and did not observe evidence that differentials in male-to-female ratios among stillbirths by race/ethnic group were substantially different across gestational ages (►Supplementary Tables S4 and S5, available in the online version).

Given that the male-to-female ratio in early versus late gestational ages for blacks could be interpreted as too few males surviving to 20 weeks' gestation, this indicates that the substantially observed elevated population prevalence (relative to other race/ethnic groups) of spontaneous PTB among blacks would show an even larger magnitude disparity compared with whites. Hypothetically, it seems unlikely that the alternative inference is operative, that is, female black infants are "escaping" miscarriage and thus increasing the prevalence of PTB.

Racial differences, that is, between whites and blacks, in secondary sex ratios at birth have been recognized for decades, although only indirectly[25] as potential clues to spontaneous PTB. Khoury et al investigated U.S. birth certificate data from 1972 to 1979.[27] They observed that white fathers had more male offspring than did black fathers, controlling for mother's race.[27] A similar pattern was observed in the current data for term births but not for each gestational age preterm grouping (►Table 2). What or how father-mediated mechanisms might contribute to this male-to-female differential by race is unknown.

Our study has several strengths including its population-based design and large sample size. Our study also had challenges typical of the nature of administrative data sources. Namely, the depth of information is limited to explore more detailed associations. Our ability to define spontaneous PTB relied on ICD-9 codes. Such reliance may result in errors in estimating associations, errors likely leading toward attenuation of the observed associations. The most important limitation, although not particularly unique to our study, is that secondary sex ratio is inferentially fraught owing to the absence of information on all conceptions, that is, the at-risk population.

Our study rigorously adds to the scant literature on this topic. Our observations offer a potential new line of inquiry toward trying to disentangle the complex etiology that seems to underlie the elevated risks of spontaneous PTB among U.S. blacks.

Note

The data are publicly available from the Office of Statewide Health Planning and Development (OSHPD). The data are not available for replication because specific approvals from OSHPD and the California Committee for the Protection of Human Subjects must be obtained to access them.

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Conflict of Interest

None declared.

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