Birthweight and Cardiometabolic Risk Patterns in Multiracial Children

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Abstract

BACKGROUND/OBJECTIVES—Prenatal growth, which is widely marked by birthweight, may play a pivotal role in affecting the lifelong risk of cardiometabolic disorders; however, comprehensive evaluation of its relations with childhood cardiometabolic risk patterns and the ethnic and gender disparities in national representative populations is still lacking. The aim of this study was to evaluate the associations between birthweight and comprehensive patterns of cardiometabolic risk in a nationally representative sample of children and adolescents.

SUBJECTS/METHODS—Prospective analyses were performed using data from 28,153 children 0 to 15 years in the National Health and Nutrition Examination Survey (NHANES) from 1999 through 2014. We defined childhood cardiometabolic disorders using standard definitions for obesity, high blood pressure, hyperglycemia, and dyslipidemia.

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RESULTS—Five birthweight categories <2.5, 2.5–3.0, 3.0–3.5, 3.5–4.2, and 4.2 kg accounted for 8.2%, 17.9%, 35.7%, 27.9%, and 10.4% of the population, respectively. In all children, with increasing birthweight, we observed significantly increasing trends of the risk of general and central obesity (p for trend < 0.01), and significantly decreasing trends of the risk of high SBP, high HbA1c, and low HDL-C (p for trend < 0.05). The associations were independent of current BMI. In addition, we found that the relations of birthweight with high waist circumference in black children showed U-shape, as well as high SBP in Mexican and Hispanic children. Moreover, we found that the associations of low birthweight with high SBP and low HDL-C appeared to more prominent significant in boys, while the inverse association with high HbA1c was more evident in girls.

CONCLUSIONS—Our data indicate that birthweight is significantly related to childhood cardiometabolic risk, independent of current BMI; and the associations exhibit race and gender-specific patterns.

Keywords

birthweight; childhood cardiometabolic risks; multiracial children

INTRODUCTION

Compelling evidence has shown that prenatal growth may play a pivotal role in affecting fetal metabolism and organ structure, and subsequently influence health after birth.[1–4] In epidemiological studies, low birthweight (LBW), a widely used indicator for prenatal growth retardation caused by intrauterine malnutrition or other stress, has been consistently associated with increased risk of a variety of cardiometabolic disorders such as type 2 diabetes (T2D) and cardiovascular disease (CVD) in adults.[5–9]

Adulthood cardiometabolic risks have their origin in childhood; and childhood obesity, high blood pressure, hyperglycemia, and dyslipidemia have been found to predict cardiometabolic diseases in adults.[10–12] In the U.S., the prevalence of obesity and cardiometabolic disorders has been rapidly increasing in children and adolescents.[13] However, few studies have comprehensively assessed the relations between birthweight and overall cardiometabolic risk patterns in children from nationally representative populations. In addition, previous studies in adults suggest that the effects of birthweight may be partly through affecting body weight after birth; it remains unclear whether birthweight is independently related to childhood cardiometabolic risk.[14,15]

In this study, we performed prospective analyses on associations between birthweight and comprehensive patterns of cardiometabolic risk in a nationally representative sample of children and adolescents from the National Health and Nutrition Examination Survey (NHANES). We particularly compared the association patterns across different race groups, and between girls and boys.

MATERIALS AND METHODS

Study design and data sources

The NHANES is a nationally representative cross-sectional survey of civilian non-institutionalized U.S. population. The NHANES includes two phases: personal interviews at home on a variety of health topics and demographic information, and standardized physical examinations and laboratory tests at a mobile examination center (MEC). Signed informed consent was obtained from all participants attended both phases, and data are publicly available. This study was deemed exempt from human subjects approval by the Institutional Review Board of the School of Public Health and Tropical Medicine at the Tulane University. Data were obtained from the public-release data sets of the most recent eight NHANES circles (NHANES survey conducted every two years since 1999), with NHANES 1999–2000 as the first and NHANES 2013–2014 the most recent. We included subjects who were both interviewed at home and received an MEC examination (N=78,518). Among them, only children aged 0 to 15 years were with available birthweight information (N=29,758). After an exclusion of individuals with missing data on birthweight or for whom birthweight was under 1.00 pound or above 13 pounds, a total number of 28,679 children were included in the current study. The demographic characteristics are shown in Table S1.

Birthweight

Information about birthweight in NHANES 1999–2014 was collected through an in-home interview, children 0 to 15 years of age at the time of examination. Participants were asked to report their birthweight in pounds and ounces. For those who were too young or unable to answer, birthweight was responded by their parents or guardians. We converted birthweight into kilograms, and generated birthweight groups with five categories (<2.5, 2.5–3.0, 3.0–3.5, 3.5–4.2, and 4.2 kg), given <2.5kg as a LBW group and 4.2 kg as high birthweight (HBW) group.[16] Extreme birthweight were excluded (<0.45 kg or 5.90 kg).

Covariates

Demographic information were all self-reported or responded by parents or guardians during the in-home interviews, including age at screening, gender (male or female), race (Non-Hispanic White; Non-Hispanic Black; Mexicans and Hispanics; Other race including Multi-Racial), and the ratio of family income to poverty (calculated by dividing family income to family size, ranging from 0.00 to 5.00). Additionally, maternal smoking status was also included, defined as (1) no smoking during the entire pregnancy; (2) quit smoking in the first trimester of pregnancy; (3) quit smoking in the second trimester of pregnancy; (4) quit smoking in the third trimester of pregnancy; (5) kept smoking throughout the entire pregnancy.

Childhood cardiometabolic disorders

Eleven measured variables related to known cardiometabolic risks were examined in children, with the definition of abnormal values shown in Table 1. Detailed information about physical examination and laboratory procedures can be found with online documentary manuals of "Laboratory Methods" and "Examination and Laboratory

Procedures" of every NHANES circles from 1999 to 2014, from the official website (http://www.cdc.gov/nchs/nhanes.htm).

Obesity—Waist circumference (WC) was measured at the time of the physical examination for all children (n=28,153), whereas standing height for children was measured only in those two years of age or over. We defined abnormal values of body mass index (BMI) as any value that was 95th percentile specific for age and gender, derived from the Clinical Growth Charts from Centers for Disease Control and Prevention (CDC).[17] The abnormal values of WC and weight were defined as 90th percentile specific for age and gender, in accord with the recommendations by the International Diabetes Federation (IDF).[18]

High blood pressure—Up to three consecutive blood pressure measurements were recorded on all examinees aged eight years and older. Blood pressure was calculated as the mean value of up to three consecutive measurements in the MEC (86% of the children had three measurements, 8% had two, and 6% had one). Abnormal values of both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were defined as any value that was 95th percentile specific for age, gender, and height derived from the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents.[19]

Hyperglycemia—Glycemic profile was obtained with two laboratory variables, including glycated hemoglobin (HbA1c) for participants aged 12 years and older and fasting blood glucose (FBG) in the subgroup who examined in the morning examination session. Any participant with a history of diabetes or antidiabetic medication was removed from the analysis of HbA1c and FBG, and an additional requirement for participants with fasting hours between 8 hours and 24 hours was applied to the analysis of FBG. Hyperglycemia in children and adolescents were defined as high FBG (100 mg/dL) and high HbA1c (> 5.7%), according to the recommendation from ADA (American Diabetes Association)[20], AHA (American Heart Association),[21] IDF,[22] NHLBI (National Heart, Lung, and Blood Institute),[23] and AAP (American Academy of Pediatrics).[24]

Dyslipidemia—Complete lipid profile was obtained, including non-fasting total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) on participants three years of age or over. Fasting triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) were available in the subgroup of who attended the morning examination session in NHANES 1999–2012. Participants whose fasting hours less than 8.5 hours or exceeding 24 hours were excluded from the analysis of TG and LDL-C. Dyslipidemia was defined as high TG (150 mg/dL), high TC (200 mg/dL), low HDL-C (< 35 mg/dL), or high LDL-C (130 mg/dL).[21–24]

Each cardiometabolic risk factor variable varies due to specialized sampling frame and examination requirements in NHANES; detailed information of analysis sample size is shown for all children, boys, and girls by race in Table S3.

Statistical Analysis

In the current study, all reported results and statistical tests were accounted for the NHANES survey design (the primary sampling units and strata) and sample weights (two-year sample

weights for participants who both interviewed and MEC examined) for the unequal probabilities of selection, nonresponse and adjustment to independent population controls. Stratified analysis was performed by gender, by race/ethnicity, and by gender and race group. The estimated prevalence of each cardiometabolic disorder was calculated with 95% confident intervals (95% CI) in five ordinal birthweight categories. For further adjustments, we performed survey-weighted generalized linear models to estimate odds ratios (ORs) for each cardiometabolic disorders by birthweight categories, controlling for age, gender, race/ethnicity, the ratio of family income to poverty, maternal smoking status and the NHANES circles (model 1). Besides covariates mentioned above, we subsequently explored whether the associations of birthweight with each cardiometabolic disorders were affected through current BMI (model 2). Linear and non-linear trends were tested by introducing an ordinal variable of birthweight categories and the quadratic term into the model, respectively. All data management and analysis were conducted using R version 3.2.3 (Wooden Christmas-Tree). For analysis of complex survey samples, the R package named "Survey" was introduced to produce nationally representative estimates, with inverse-probability weighting and design-based standard errors.[25–27] Statistical significance was assessed at the 2-sided α=0.05 level.

RESULTS

Baseline characteristics

Among 28,679 children 0 to 15 years of age (50.9% were boys; 57.2% were Non-Hispanic Whites), 8.2% were born at LBW (Figure 1), with the highest proportion of LBW in Blacks (14.0%) and the lowest in Whites (6.5%). The mean birthweight was 3.32±0.61 kg in all children, 3.13±0.66 kg in Non-Hispanic Black children, 3.31±0.61 kg in Mexicans & Hispanics, and 3.32±0.62 kg in Whites (Figure S1). On average, boys were born 0.1 kg heavier than girls (Figure S1 and Table S2). In NHANES, ten cardiometabolic traits (except for body weight) were available in sub-samples (8.6~79.9% of the whole sample) with varying age ranges (Table 1).

Cardiometabolic risk patterns by five birthweight categories

In all children, boys and girls (Figure 2), we observed consistently and significantly increasing trends of prevalence of high WC, whereas significantly decreasing trends of prevalence of high SBP and high HbA1c with increasing birthweight. Of note, in Mexican and Hispanic children, the prevalence and ORs of high SBP, and low HDL-C showed U-shaped relationships with birthweight. As WC, BMI, and weight were highly correlated obesity markers, we found the similar prevalence trends and association patterns of birthweight with BMI and weight (Figure S2–S4, and Table S4 and S6). No clear trends were observed for prevalence of high DBP, high FBG, high TG, high TC, and high LDL-C according to birthweight in the whole population, in each race groups, and in boys and girls (Figure S2–S4, and Table S8, S9, S11, S12, and S14).

Difference in association patterns with and without adjustment for current BMI

We further found that the risk patterns of four cardiometabolic disorders (high WC, SBP, and HbA1C and low HDL-C) with birthweight groups showed significant difference with and

without adjustment for current BMI (Figure 3). Consistent with prevalence association patterns in Figure 2, Figure 3 showed similar linear trend of ORs for the associations of birthweight with high WC (P<0.001) and high SBP (P=0.034), but not with high HbA1c (P=0.090) and low HDL-C (P=0.236) in models without adjustment for BMI in all children. We found that additional adjustment for current BMI significantly improved the inverse associations of birthweight with high HbA1c and HDL-C (P=0.010 and 0.004, respectively); while the associations with high WC and SBP remained significant. In addition, the sensitivity analyses, by limiting our study sample into children with a normal birthweight of 2.5~4.2 kg (data not shown), also showed similar associations between birthweight (kg) and cardiometabolic risks (ORs: 1.35, 0.59, 0.79, and 0.76 for high WC, high SBP, high HbA1c, and low HDL-C, respectively).

Ethnical difference in cardiometabolic risk patterns by five birthweight categories

In figure 2 and 3, significant ethnical difference were shown and tested (all p<0.05) in the association patterns of cardiometabolic risk patterns with birthweight, we then performed similar analyses in each race group. Of interest, after adjustment for current BMI, the linear association between birthweight and high WC turned into a U-shape in black children (P_{trend}<0.001 vs. $P_{non-linear\ trend}$=0.061), whereas the U-shaped relation of birthweight with low HDL-C turned into a linear pattern in Mexican & Hispanic children ($P_{non-linear\ trend}$=0.003 vs. P_{trend}=0.001).

Gender difference in cardiometabolic risk patterns by five birthweight categories

We also analyzed the associations in boys and girls separately (Table 2). Except for high WC, the inverse trends of ORs were not significant in models without adjustment for current BMI among both boys and girls. After adjustment for current BMI, the inverse associations of birthweight with high SBP and low HDL-C became significant in boys, similar with the trends of ORs for high HbA1c in girls. Adjustment for current BMI did not appreciably change the relation between birthweight and high WC.

DISCUSSION

In this prospective study of a nationally representative children and adolescent sample, we found that birthweight, a widely-used marker of prenatal growth, was significantly and positively associated with a higher risk of general and central obesity, while significantly and negatively associated with cardiometabolic disorders including high SBP, high HbA1c, and low HDL-C, independent of current body size. The relations of birthweight with childhood cardiometabolic disorders showed different patterns by race and gender.

Our findings are in line with previous findings in children and adolescents. A meta-analysis[28] showed a 1.76 (1.65–1.87) fold higher risk of overweight with high birthweight (>4.0 kg) among 643,902 participants under 18. Two systematic reviews by Huxley[29] and Law[30] noted that a lower birthweight was significantly associated with an higher SBP in adolescence. Birthweight has been consistently related to cardiometabolic risk in adults, but with relatively smaller effect sizes on obesity and SBP compared with in children and adolescents.[28–30] Growing evidence revealed that people who were born with LBW had a

higher risk of T2D in a later life.[7,9] Nevertheless, regarding the association of birthweight with specific glycemic and lipid profiles, the existing data appeared to be conflicting in both children and adults.[5,15,31] Two previous studies[32,33] reported that there was no difference in HbA1c levels between LBW and non-LBW group, but both studies were based on analyses among childhood-onset T2D patients. A lower HDL-C level was observed in LBW group in two adults based studies;[34,35] however, such difference did not reach significant levels, probably due to insufficient power. Additionally, the thus-far largest genome-wide association study[36] demonstrated that genetic factors were the major contributor to the negative association between birthweight and future cardiometabolic risk. Our data suggested that higher birthweight might particularly improve SBP, HbA1c, and HDL-C levels, regardless elevated adiposity, in children.

Birthweight is fundamentally determined by *in utero* environment. According to the theory of the developmental origins of health and disease (DOHaD),[3,37] the life-long risk of major adult-onset cardiometabolic diseases has its origin in prenatal development. Previous studies in adults consistently support detrimental effects of LBW that indicates impaired intrauterine growth.[9,38,39] Our data indicates that such adverse effects of LBW may start from early life. Impaired intrauterine growth may affect "metabolic programming"[40,41] and structure of organs and tissues,[4,42,43] which result in irreversible long-term adverse effects on cardiometabolic health[3,41]. For example, LBW could contribute to an elevated blood pressure via affecting the hypothalamic– pituitary–adrenal (HPA) axis regulation, renal injury, oxidative stress and inflammation, nutrition, and glucocorticoids.[3,44,45] Furthermore, LBW infants are subject to leptin resistance and insulin resistance, which may lead to defects in glycemic homeostasis such as elevated HbA1c.[1,4,46] Nevertheless, our data and sensitivity analyses suggested participants born with a higher birthweight may carry the cardiometabolic risk associated with general and abdominal obesity, but may be protected against insulin resistance and dyslipidemia, probably owing to a greater lean mass[47], undisturbed glucose homeostasis[48], or an appropriate gestational age[49], compared with LBW. The divergent associations of birthweight with obesity and other cardiometabolic disorders including high SBP, high HbA1c, and low HDL-C suggest that the effects of birthweight on these cardiometabolic disorders may be independent of adiposity. An alternative hypothesis is that LBW infants experience "catch-up" growth in the first months after birth when a "mismatch" between the prenatal and postnatal environment occurs,[4] whereas HBW infants might experience growth deceleration. Such differences during the critical stage of development may have lasting influence on cardiometabolic health.[4,49]

Intriguingly, we noted the U-shaped relations of birthweight with high WC and high SBP in black and Mexican & Hispanic children, respectively. We speculated the combination of LBW and rapid postnatal catch-up growth contributed to an increased risk of abdominal obesity in black children[50], due to a well-documented lower birthweight compared with whites, as well as diet-related disparities, a less nutritious, calorie-dense food environment because of a lower family incomes and poverty.[51] Though the underlined mechanism is not well-defined, excessive glucocorticoid exposure, rapid postnatal growth, and enhanced insulin secretion/action in LBW children were considered to participate in the increased visceral/abdominal fat.[52–54] Additionally, the significant "J" or "U" shaped relations between birthweight and cardiometabolic disorders were more frequently observed in non-

European populations.[8,28,55–58] These observations, together with ours, suggest that the effects of birthweight on cardiometabolic risk patterns may differ according to racial background. We assume that diversity in genetic predispositions and varying environment among different racial populations may partly account for such disparities, though more studies are warranted to explore the potential mechanisms.

In addition, we found the cardiometabolic risk associated with birthweight showed gender-specific patterns, boys born lighter appeared to have an elevated SBP and lower HDL-C level, while girls born at HBW showed a higher risk of adulthood obesity.[58] Such gender-specific relations were also previously reported in both children and adults. A cross-sectional study of 5,141 children aged 9–11 years conducted in 12 countries found that a positive association of birthweight and the odds of childhood obesity was noted in girls, whereas a U-shaped relation seen in boys.[59] Similarly, our stratified analyses showed a significant U-shaped relationship of WC with birthweight only in the black boys after adjusting for BMI (p=0.035), but not in girls (Table S5). This founding might indicate that, African American boys, compared with girls, are more vulnerable to prenatal growth retardation for its later adverse impact on the accumulation of visceral/abdominal adiposity. Results from a prospective analysis on 197,954 adults from 20 Nordic cohorts showed a significant inverse linear trend of SBP with birthweight in men, while a non-linear trend in women.[60] Sex hormones may play a critical role in "programming" the gender-specific response to abnormal fetal growth[45] and subsequent cardiometabolic risk, whereas other mechanisms are also likely to be involved.

In the current study, we used a nationally representative sample to evaluate the association between birthweight and multiple cardiometabolic disorders in childhood. To our knowledge, this study including eight circles of NHANES since 1999 had thus far the largest sample size of children and adolescent to study the effects of birthweight on cardiometabolic risk patterns, Further, because NHANES had kept a high response rate, strict quality control, and data cross-validation, potential bias due to population selection and measurement errors were minimized. Even though, several limitations merit discussion. First, information about birth weight was collected through interview of participants or their parents or guardians, not from the birth records. Second, small sample size in some subgroups resulted in wide confidence intervals and missings coefficients due to little cases. Third, although we had carefully controlled for covariates in our analyses, information on some potential confounders was unavailable (such as gestation period, breastfeeding duration, gestational BMI and weight gain, childhood puberty, dietary intake, and physical activity), making us unable to control for their influence on the associations. In addition, childhood high blood pressure and dyslipidemia were measured in certain age range of study samples, which might limited the generaliztion of what we found.

In summary, birthweight was significantly associated with overall cardiometabolic risk patterns including obesity, high SBP, high HbA1c, and low HDL-C in childhood and adolescence, and such associations showed race- and gender-specific patterns. Our findings reemphasize the point that adulthood cardiometabolic risk associated with prenatal growth retardation may have its origin in childhood and highlight the importance of life-course prevention on cardiometabolic disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations list

BMI	body mass index
DBP	diastolic blood pressure
DOHaD	the developmental origins of health and disease
FBG	fasting blood glucose
HbA1c	glycated hemoglobin A1c
HDL-C	high-density lipoprotein cholesterol
LBW	low birthweight
LDL-C	fasting blood low-density lipoprotein cholesterol
SBP	systolic blood pressure
TC	total cholesterol
TG	fasting blood triglyceride
WC	waist circumference

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(a). Boys

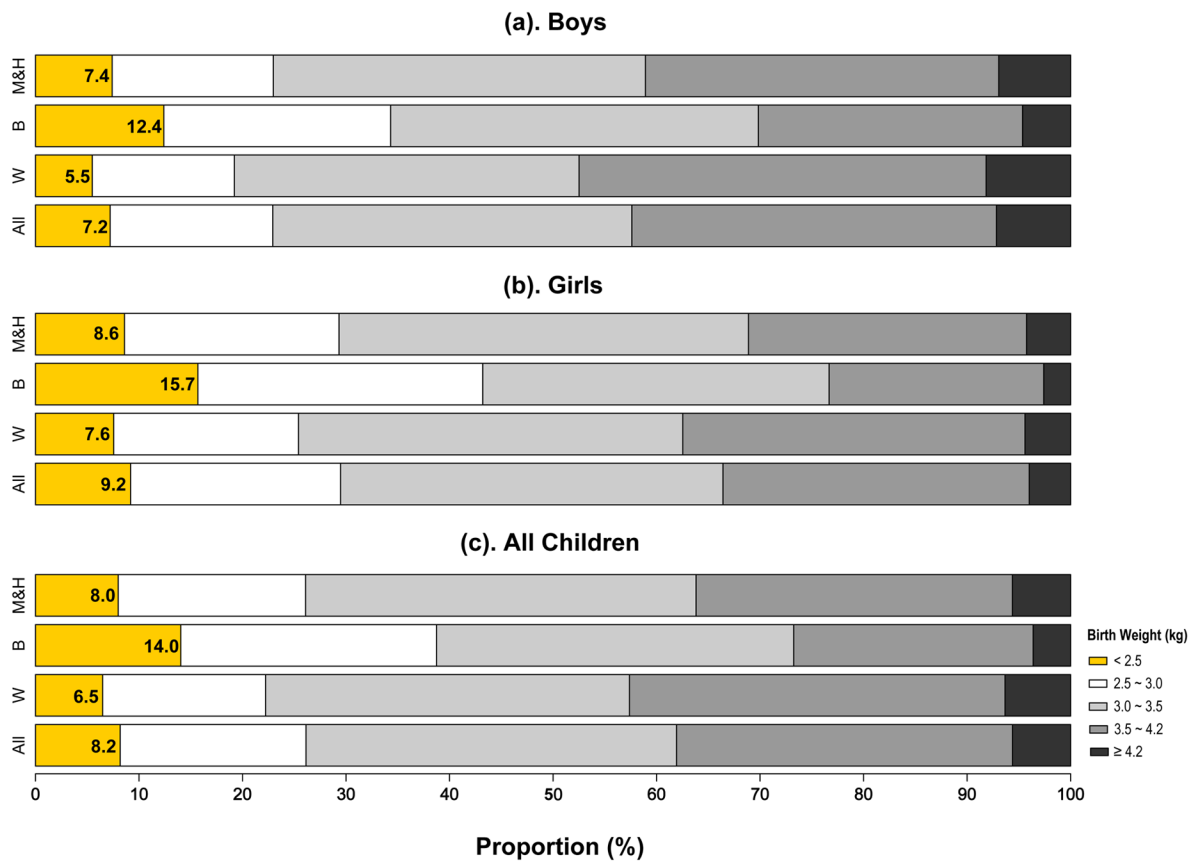## (b). Girls

(c). All Children

Figure 1. Proportion of Low birth weight in boys and girls, and all children by three different race/ethnic groups

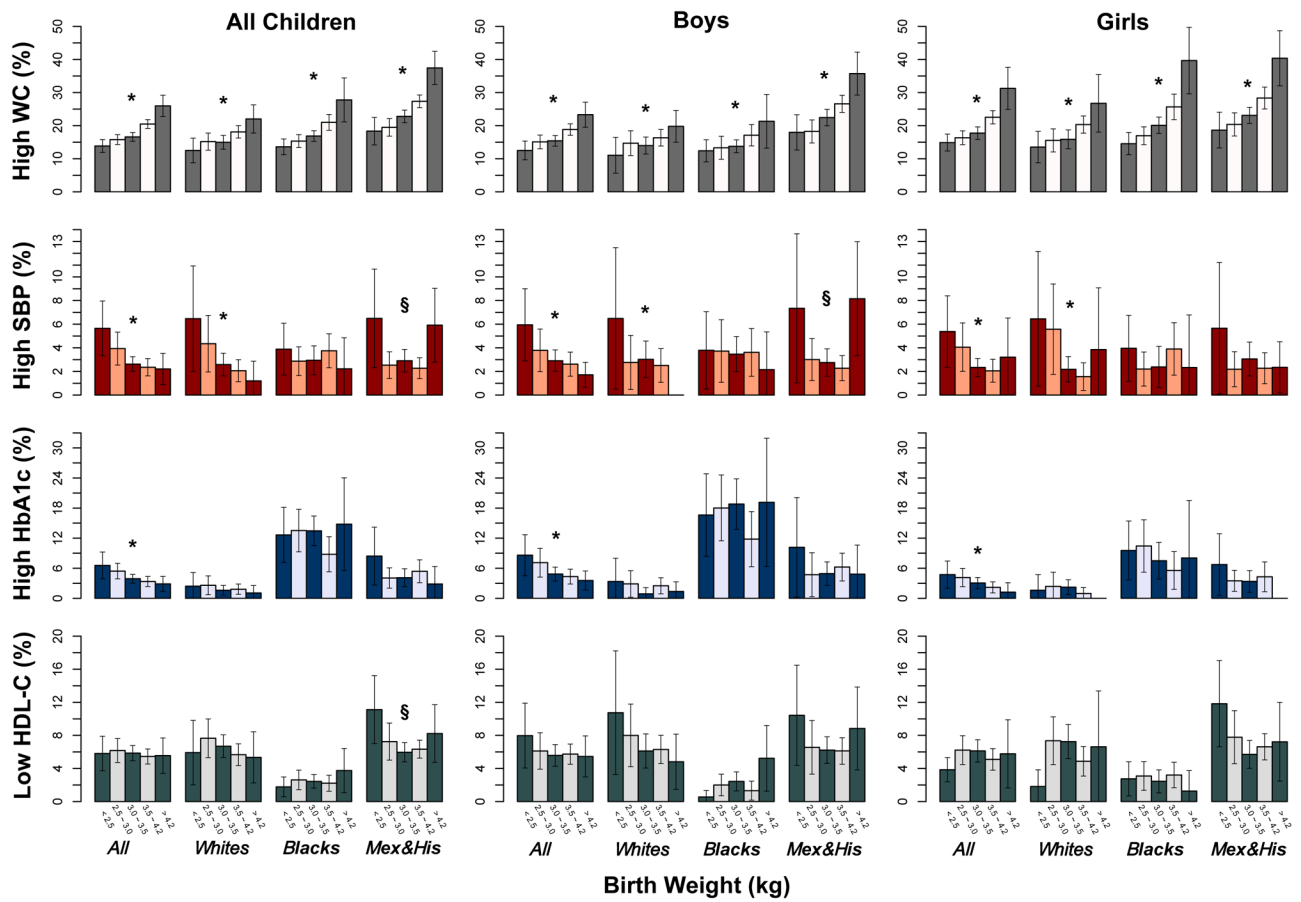W, Non-Hispanic Whites; B, Non-Hispanic Blacks; Mex & His, Mexicans and Other Hispanics.

Figure 2. Prevalence of Four Cardiometabolic risk factors by birth weight in all children, boys and girls by three different race/ethnic groups[*]

P for linear trend <0.05; [§], P for non-linear trend <0.05; W, Non-Hispanic Whites; B, Non-Hispanic Blacks; Mex & His, Mexicans and other Hispanics.

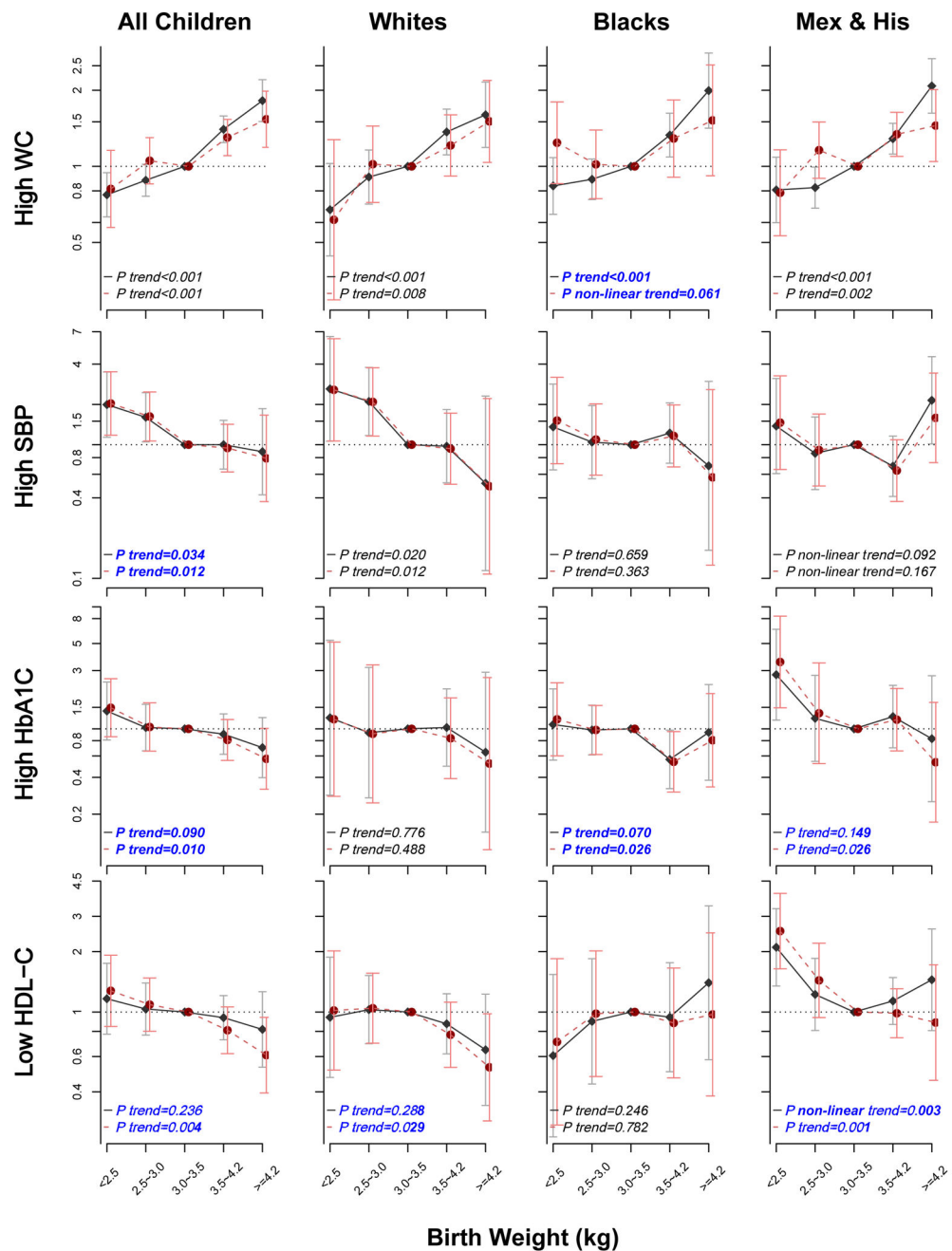**Figure 3. Odds Ratios of Four Cardiometabolic risk factors by birth weight in all children, and three race groups**

Model 1 with solid line, adjusted for survey-weighted logistic regression models that controlled for age, ethnic group, gender, NHANES circles, family income, and maternal smoking status; Model 2 with dotted line, adjusted for BMI and covariates in Model 1. P trend represented the significance of linear trend test.

Table 1

Sample Size and Definition of Abnormal Values for Cardiometabolic Risk-Factor Variables. [*]

Variable	Age Range (yrs.)	Sample Size (n, %)	Definition of Abnormal Value
Glycemic profile			
FBG	12 – 15	2410 (8.6)	100 mg/dL
HbA1c	12 – 15	6077 (21.6)	>5.7%
Blood Pressure			
SBP	8 – 15	12199 (43.3)	95th percentile[#]
DBP	8 – 15	12200 (43.3)	95th percentile[#]
Blood Lipids			
TG	3 – 15	3208 (11.4)	150 mg/dL
TC	3 – 15	14409 (51.2)	200 mg/dL
HDL-C	3 – 15	14407 (51.2)	<35 mg/dL
LDL-C	3 – 15	3193 (11.3)	100 mg/dL
Body Mass Measurements			
BMI	2 – 15	22495 (79.9)	95th percentile[§]
Waist	2 – 15	21633 (76.8)	90th percentile[§]
Weight	0 – 15	28153 (100%)	90th percentile[§]

[*] Data are shown for children under 16 years old. FBG, fasting blood glucose; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, fasting blood triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, fasting blood low-density lipoprotein cholesterol; BMI, body mass index; Whites, Non-Hispanic White; Blacks, Non-Hispanic Black; Mex & His, Mexicans and Other Hispanics.

[#] Age-, gender- and height-specific cutoff value.

[§] Age- and gender-specific cutoff value.

Table 2

Odds Ratios for Four Cardiometabolic risk factors by birth weight in boys and girls by Birth Weight Category.[*]

Birth Weight Category	Boys		Girls	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
High WC				
<2.5	0.75 (0.56, 1.01)	0.76 (0.50, 1.16)	0.76 (0.58, 1.00)	0.84 (0.52, 1.36)
2.5~3.0	0.88 (0.71, 1.10)	1.08 (0.83, 1.40)	0.86 (0.72, 1.03)	1.03 (0.76, 1.39)
3.0~3.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
3.5~4.2	1.43 (1.19, 1.72)	1.40 (1.13, 1.72)	1.43 (1.20, 1.71)	1.23 (0.97, 1.54)
4.2	1.77 (1.38, 2.27)	1.36 (0.95, 1.97)	2.17 (1.58, 2.99)	2.04 (1.36, 3.06)
	P<0.001	*P= 0.002*	*P<0.001*	*P= 0.003*
High SBP				
<2.5	2.08 (1.13, 3.84)	2.18 (1.21, 3.91)	1.79 (0.82, 3.94)	1.83 (0.83, 4.03)
2.5~3.0	1.30 (0.68, 2.49)	1.33 (0.70, 2.56)	1.85 (0.99, 3.46)	1.86 (0.99, 3.48)
3.0~3.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
3.5~4.2	1.15 (0.66, 2.02)	1.04 (0.59, 1.84)	0.86 (0.48, 1.52)	0.84 (0.47, 1.48)
4.2	0.72 (0.32, 1.61)	0.62 (0.28, 1.38)	1.30 (0.40, 4.29)	1.20 (0.36, 4.01)
	P= 0.126	*P= 0.037*	*P= 0.087*	*P= 0.063*
High HbA1c				
<2.5	1.67 (0.85, 3.28)	1.73 (0.89, 3.38)	1.17 (0.57, 2.39)	1.27 (0.63, 2.57)
2.5~3.0	1.08 (0.59, 1.99)	1.09 (0.58, 2.06)	1.04 (0.54, 2.01)	1.05 (0.54, 2.05)
3.0~3.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
3.5~4.2	1.05 (0.64, 1.71)	0.95 (0.58, 1.58)	0.75 (0.38, 1.49)	0.68 (0.34, 1.35)
4.2	0.90 (0.50, 1.62)	0.84 (0.46, 1.53)	0.38 (0.08, 1.89)	0.20 (0.04, 1.00)
	P= 0.265	*P= 0.119*	*P= 0.123*	*P= 0.018*
Low HDL-C				
<2.5	1.66 (0.90, 3.03)	1.84 (0.99, 3.42)	0.71 (0.46, 1.11)	0.80 (0.52, 1.23)
2.5~3.0	1.01 (0.64, 1.62)	1.11 (0.69, 1.79)	1.03 (0.73, 1.44)	1.06 (0.74, 1.51)
3.0~3.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
3.5~4.2	1.03 (0.74, 1.44)	0.89 (0.62, 1.28)	0.86 (0.61, 1.22)	0.71 (0.47, 1.07)
4.2	0.73 (0.41, 1.33)	0.59 (0.32, 1.08)	0.95 (0.45, 1.99)	0.67 (0.32, 1.38)

Birth Weight Category	Boys		Girls	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
	P= 0.171	*P= 0.020*	*P= 0.927*	*P= 0.085*

*
P value was given for the statistical significance of the linear trend test of odds ratios among five ordinal birthweight categories.

[a]Model 1, survey-weighted logistic regression models that controlled for age, ethnic group, NHANES circles, family income, and maternal smoking status.

[b]Model 2 = Model 1 + BMI.